This is a digital copy of a book that was preserved for generations on library shelves before it was carefully scanned by Google as part of a project to make the world's books discoverable online.

It has survived long enough for the copyright to expire and the book to enter the public domain. A public domain book is one that was never subject to copyright or whose legal copyright term has expired. Whether a book is in the public domain may vary country to country. Public domain books are our gateways to the past, representing a wealth of history, culture and knowledge that's often difficult to discover.

Marks, notations and other marginalia present in the original volume will appear in this file - a reminder of this book's long journey from the publisher to a library and finally to you.

Usage guidelines

Google is proud to partner with libraries to digitize public domain materials and make them widely accessible. Public domain books belong to the public and we are merely their custodians. Nevertheless, this work is expensive, so in order to keep providing this resource, we have taken steps to prevent abuse by commercial parties, including placing technical restrictions on automated querying.

We also ask that you:

+ *Make non-commercial use of the files* We designed Google Book Search for use by individuals, and we request that you use these files for personal, non-commercial purposes.

+ *Refrain from automated querying* Do not send automated queries of any sort to Google's system: If you are conducting research on machine translation, optical character recognition or other areas where access to a large amount of text is helpful, please contact us. We encourage the use of public domain materials for these purposes and may be able to help.

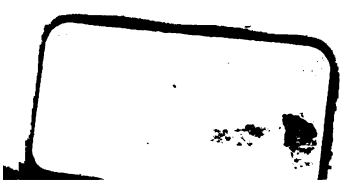
+ *Maintain attribution* The Google "watermark" you see on each file is essential for informing people about this project and helping them find additional materials through Google Book Search. Please do not remove it.

+ *Keep it legal* Whatever your use, remember that you are responsible for ensuring that what you are doing is legal. Do not assume that just because we believe a book is in the public domain for users in the United States, that the work is also in the public domain for users in other countries. Whether a book is still in copyright varies from country to country, and we can't offer guidance on whether any specific use of any specific book is allowed. Please do not assume that a book's appearance in Google Book Search means it can be used in any manner anywhere in the world. Copyright infringement liability can be quite severe.

About Google Book Search

Google's mission is to organize the world's information and to make it universally accessible and useful. Google Book Search helps readers discover the world's books while helping authors and publishers reach new audiences. You can search through the full text of this book on the web at `http://books.google.com/`

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE
HARVARD MEDICAL LIBRARY-BOSTON MEDICAL LIBRARY



TRANSACTIONS

OF THE

ASSOCIATION OF AMERICAN PHYSICIANS.

SIXTH SESSION,

HELD AT WASHINGTON, D. C.,

SEPTEMBER 22, 23, 24, AND 25, 1891.

VOLUME VI.

PHILADELPHIA:
PRINTED FOR THE ASSOCIATION.
1891.

CONTENTS.

	PAGE
List of officers for the year 1891–92	v
List of honorary members	vi
List of members	vii
Constitution	xi
Minutes of the Sixth Annual Meeting	xiv

I. Treatment of Visceral Tuberculosis by Koch's Method. By FRANCIS P. KINNICUTT, M.D., Physician to St. Luke's Hospital, New York 1

II. "Tuberculin and Tuberculosis." By HAROLD C. ERNST, M.D., Physician to Out-patients, Massachusetts General Hospital; Assistant Professor of Bacteriology in Harvard University . 15

III. Koch's Treatment of Tuberculosis. By WILLIAM OSLER, M.D., Professor of Medicine in Johns Hopkins University . . 35

IV. The Frequency of the Localization of Phthisis Pulmonalis in the Upper Lobes. By J. WEST ROOSEVELT, M.D., Physician to the Roosevelt and Bellevue Hospitals, New York . 37

V. On Certain Arrangements made in the City of Glasgow, 1866, with a view to the Prevention of Epidemic Cholera. With an Appendix. By W. T. GAIRDNER, M.D, LL.D., Professor of Medicine in the University of Glasgow, Scotland . . 56

VI. The Remote Results of the Removal of the Ovaries and Tubes. By WILLIAM T. LUSK, M.D., Professor of Obstetrics in Bellevue Hospital Medical College, New York . . . 75

VII. The Remote Results of Removal of the Ovaries and Tubes. By WHARTON SINKLER, M.D., Physician to the Infirmary for Nervous Diseases, Philadelphia, and Neurologist to the Philadelphia Hospital 86

VIII. On the Remote Results of the Removal of the Ovaries and Tubes. By JAMES J. PUTNAM, M.D., Instructor in Diseases of the Nervous System, Harvard University . . . 105

IX. Nerve-stretching in Inveterate Trigeminal Neuralgia. By JAMES STEWART, M.D., Professor of Pharmacology and Therapeutics in McGill University, Montreal . . . 119

PAGE

X. On the Diseases of the Kidneys Popularly Called "Bright's Disease." By FRANCIS DELAFIELD, M.D., LL.D., Professor of Medicine in the College of Physicians and Surgeons, New York 124

XI. Relations Between Arterial Disease and Visceral Changes. By GEORGE L. PEABODY, M.D., Professor of Materia Medica and Therapeutics in the College of Physicians and Surgeons, New York 154

XII. On the Relations Between Arterial Disease and Tissue Changes. By WILLIAM T. COUNCILMAN, M.D., of Baltimore . . 179

XIII. Intestinal Perforation in Typhoid Fever: its Prognosis and Treatment. By REGINALD H. FITZ, M.D., Shattuck Professor of Pathological Anatomy in Harvard University; Physician to the Massachusetts General Hospital . . 200

XIV. The Relations of Drinking-water to Disease. By HENRY P. WALCOTT, M.D., Cambridge, Mass. 216

XV. The Pathology of Pernicious Anæmia. By J. P. CROZER GRIFFITH, M.D., Clinical Professor of Diseases of Children in the University of Pennsylvania, and CHARLES W. BURR, M.D., of Philadelphia 239

XVI. The Conditions and Prospects of the Library of the Surgeon-General's Office, and of its Index Catalogue. By JOHN S. BILLINGS, M.D., Surgeon United States Army 251

XVII. A Case of Slow Pulse. By D. W. PRENTISS, M.D., of Washington, D.C. With the Report of the Autopsy. By ROBERT T. EDES, M.D., of Washington, D. C. 258

XVIII. Exhibition of Specimens of Hair Showing Discoloration from Internal Use of Pilocarpine and Jaborandi. By D. W. PRENTISS, M.D., of Washington, D. C. 262

XIX. On Changes in the Red Blood-corpuscles in the Pernicious Anæmia of Texas Cattle Fever. By THEOBALD SMITH, Ph.B., M.D., of Washington, D. C. 263

XX. Grave Forms of Purpura Hæmorrhagica. By J. H. MUSSER, M.D., Assistant Professor of Clinical Medicine, University of Pennsylvania 279

XXI. Bradycardia (Bradysphygmie-Ozanam) in Acute Rheumatism. By I. E. ATKINSON, M.D., Professor of Materia Medica and Therapeutics and of Clinical Medicine in the University of Maryland 292

XXII. The Climate of Southern California for Respiratory Diseases. A Preliminary Paper. By NORMAN BRIDGE, A.M., M.D., Professor of Clinical Medicine, etc., in Rush Medical College, Chicago 305

XXIII. Report of Two Cases of Epilepsy, with Albuminuria, Mistaken for Uræmic Convulsions. By JAMES TYSON, M.D., Professor of Clinical Medicine in the University of Pennsylvania 311

ASSOCIATION OF AMERICAN PHYSICIANS.

OFFICERS FOR THE YEAR 1891-92.

PRESIDENT.

HENRY M. LYMAN, M.D.

VICE-PRESIDENT.

GEORGE ROSS, M.D.

RECORDER.

I. MINIS HAYS, M.D.

SECRETARY.

HENRY HUN, M.D.

TREASURER.

W. W. JOHNSTON, M.D.

COUNCIL.

SAMUEL C. BUSEY, M.D.
WILLIAM H. WELCH, M.D.
WILLIAM PEPPER, M.D.
GEORGE L. PEABODY, M.D.
G. BAUMGARTEN, M.D.

HONORARY MEMBERS.

† Deceased.

†1890. BARKER, FORDYCE, M.D., New York.
1886. BILLINGS, JOHN S., M.D., U. S. A., Surgeon-General's Office, Washington, D. C.
1886. BOWDITCH, HENRY I., M.D., 113 Boylston St., Boston.
†1886. CLARK, ALONZO, M.D., New York.
1886. CLYMER, MEREDITH, M.D., 65 W. 38th St., New York.
†1886. DALTON, JOHN C., M.D., New York.
†1886. LEIDY, JOSEPH, M.D., Philadelphia.
1886. METCALF, JOHN T., M.D., 30 W. 33d St., New York.
1886. STILLÉ, ALFRED, M.D., 3900 Spruce St., Philadelphia.

MEMBERS.

* Original members.
† Deceased members.

*1886. ADAMS, J. F. A., M.D., 26 Wendell Ave., Pittsfield, Mass.
*1886. ATKINSON, I. E., M.D., 605 Cathedral St., Baltimore.
*1886. BALL, A. BRAYTON, M.D., 42 W. 36th St., New York.
*1886. BAUMGARTEN, G., M.D., 2643 Chestnut St., St. Louis.
1890. BOND, CHARLES S., M.D., 209 N. 8th St., Richmond, Ind.
1888. BRIDGE, NORMAN, M.D., 217 S. Broadway, Los Angeles, Cal.
†1886. BRUEN, EDWARD T., M.D., Philadelphia.
*1886. BUSEY, SAMUEL C., M.D., 1545 I St. (N. W.), Washington, D. C.
1889. CAREY, CHARLES, M.D., 340 Delaware Ave., Buffalo, N. Y.
*1886. CARPENTER, JOHN T., M.D., Pottsville, Pa.
*1886. CHEW, SAMUEL C., M.D., 215 W. Lanvale St., Baltimore.
*1886. COUNCILMAN, W. T., M.D., Johns Hopkins University, Baltimore.
1889. DABNEY, WILLIAM C., M.D., University of Virginia, Va.
*1886. DACOSTA, J. M., M.D., 1700 Walnut St., Philadelphia.
1888. DANA, CHARLES L., M.D., 50 W. 46th St., New York.
*1886. DANA, ISRAEL T., M.D., 181 State St., Portland, Me.
1888. DANFORTH, I. N., M.D., 294 W. Monroe St., Chicago.
*1886. DELAFIELD, FRANCIS, M.D., 12 W. 32d St., New York.
*1886. DONALDSON, FRANK, M.D., 510 Park Ave., Baltimore.
*1886. DRAPER, WILLIAM H., M.D., 19 E. 47th St., New York.
*1886. EDES, ROBERT T., M.D., Adams Nervine Asylum, Jamaica Plain, Mass.
1888. ERNST, HAROLD C., M.D., Jamaica Plain, Mass.

1890. Fisk, Samuel A., M.D., 809 16th St., Denver, Col.
*1886. Fitz, Reginald H., M.D., 18 Arlington St., Boston.
*1886. Folsom, Charles F., M.D., 15 Marlborough St., Boston.
*1886. Forchheimer, F., M.D., 160 W. 9th St., Cincinnati.
*1886. Formad, Henry F., M.D., 3535 Locust St., Philadelphia.
*1886. Gannett, William W., M.D., 274 Marlborough St., Boston.
*1886. Garland, George M., M.D., 274 Newbury St., Boston.
1889. Geddings, W. H., M.D., Aiken, S. C.
1889. Gibbes, Heneage, M.D., 16 Forest Ave., Ann Arbor, Mich.
*1886. Graham, J. E., M.D., 66 Gerrard St., Toronto, Canada.
1890. Griffith, J. P. Crozer, M.D., 123 S. 18th St., Philada.
*1886. Guitéras, John, M.D., 3731 Spruce St., Philadelphia.
1890. Hare, Hobart A., M.D., 222 S. 15th St., Philadelphia.
*1886. Hays, I. Minis, M.D., 266 S. 21st St., Philadelphia.
*1886. Henry, Frederick P., M.D., 1635 Locust St., Philada.
†1886. Howard, R. Palmer, M.D., Montreal, Canada.
†1886. Hudson, E. Darwin, Jr., M.D., New York.
*1886. Hun, Henry, M.D., 33 Elk St., Albany, N. Y.
1890. Hurd, Henry Mills, M.D., Johns Hopkins Hospital, Baltimore.
†1886. Hutchinson, James H., M.D., Philadelphia.
*1886. Jacobi, A., M.D., 110 W. 34th St., New York.
*1886. Janeway, E. G., M.D., 36 W. 40th St., New York.
†1886. Johnson, Hosmer A., M.D., Chicago.
*1886. Johnston, W. W., M.D., 1603 K St. (N. W.), Washington, D. C.
*1886. Kinnicutt, Francis P., M.D., 42 W. 37th St., New York.
1890. Latimer, Thomas S., M.D., 103 W. Monument St., Baltimore.
1888. Lewis, Morris J., M.D., 1316 Locust St., Philadelphia.
*1886. Longstreth, Morris, M.D., 1416 Spruce St., Philadelphia.
*1886. Loomis, Alfred L., M.D., 19 W. 34th St., New York.
1889. Loving, Starling, M.D., 229 E. State St. Columbus, Ohio.
*1886. Lusk, William T., M.D., 47 E. 34th St., New York.
*1886. Lyman, Henry M., M.D., 65 Randolph St., Chicago.
†1886. McBride, Thomas A., M.D., New York.
†1890. MacDonnell, R. L., M.D., Montreal, Canada.
1891. McPhedran, A., M.D., 84 College St., Toronto, Canada.

1891. MASON, A. LAWRENCE, M.D., 265 Clarendon St., Boston
1887. MEIGS, ARTHUR V., M.D., 1322 Walnut St., Philadelphia.
*1886. MILES, F. T., M.D., 514 Cathedral St., Baltimore.
*1886. MINOT, FRANCIS, M.D., 65 Marlborough St., Boston.
*1886. MITCHELL, S. WEIR, M.D., 1524 Walnut St., Philadelphia.
1887. MUSSER, JOHN H., M.D., 40th and Locust Sts., Philadelphia.
1891. NORTHRUP, W. P., M.D., 57 E. 79th St., New York.
*1886. OSLER, WILLIAM, M.D., Johns Hopkins Hospital, Baltimore.
*1886. PEABODY, GEORGE L., M.D., 57 W. 38th St., New York.
*1886. PEPPER, WILLIAM, M.D., 1811 Spruce St., Philadelphia.
*1886. POLK, WILLIAM M., M.D., 7 E. 36th St., New York.
1888. PRENTISS, D. W., M.D., 1101 14th St. (N. W.), Washington, D. C.
*1886. PRUDDEN, T. MITCHELL, M.D., 23 W. 33d St., New York.
1889. PURDY, CHARLES W., M.D., 163 State St., Chicago.
*1886. PUTNAM, JAMES J., M.D., 106 Marlborough St., Boston.
1887. REEVES, JAMES E., M.D., 201 McCallie Ave., Chattanooga, Tenn.
*1886. ROBINSON, BEVERLEY, M.D., 37 W. 35th St., New York.
*1886. ROBINSON, P. G., M.D., 3411 Washington Ave., St. Louis.
†1886. ROCHESTER, THOMAS F., M.D., Buffalo, N. Y.
1889. ROOSEVELT, J. WEST, M.D., 32 E. 31st St., New York.
*1886. ROSS, GEORGE, M.D., 49 Union Ave., Montreal, Canada.
†1886. SCHMIDT, H. D., M.D., New Orleans, La.
*1886. SEGUIN, E. C., M.D., 419 Madison Ave., New York.
*1886. SHAKESPEARE, EDWARD O., M.D., 1336 Spruce St., Philada.
*1886. SHATTUCK, FREDERICK C., M.D., 125 Marlborough St., Boston.
*1886. SHATTUCK, GEORGE B., M.D., 24 Marlborough St., Boston.
*1886. SINKLER, WHARTON, M.D., 1606 Walnut St., Philadelphia.
*1886. SMITH, A. A., M.D., 40 W. 47th St., New York.
1891. SMITH, ANDREW H., M.D., 22 E. 42d St., New York.
*1886. SOLLY, EDWIN S., 2 N. Cascade Ave., Colorado Springs, Col.
1887. STARR, LOUIS, M.D., 1818 S. Rittenhouse Square, Philada.
1887. STARR, M. ALLEN, M.D., 22 W. 48th St., New York.
*1886. STERNBERG, GEORGE M., M.D., U. S. A., Johns Hopkins University, Baltimore.

*1886. STEWART, JAMES, M.D., 939 Dorchester St., Montreal, Canada.
1889. STOCKTON, CHARLES G., M.D., 278 Franklin St., Buffalo, N. Y.
†1886. THACHER, JAMES K., M.D., New Haven, Conn.
1889. THOMPSON, W. GILMAN, M.D., 49 E. 30th St., New York.
1889. THOMSON, WILLIAM H., M.D., 7 W. 56th St., New York.
*1886. TRUDEAU, EDWARD L., M.D., Saranac Lake, Franklin Co., N. Y.
*1886. TYSON, JAMES, M.D., 1506 Spruce St., Philadelphia.
1889. VAUGHAN, VICTOR C., M.D., University of Michigan, Ann Arbor, Mich.
1889. WALCOTT, HENRY P., M.D., 11 Waterhouse St., Cambridge Mass.
*1886. WARD, SAMUEL B., M.D., 135 N. Pearl St., Albany, N. Y.
*1886. WELCH, WILLIAM H., M.D., 506 Cathedral St., Baltimore.
1889. WESTBROOK, B. F., M.D., 174 Clinton St., Brooklyn, N. Y.
*1886. WHITTAKER, JAMES T., M.D., 100 W. 8th St., Cincinnati.
*1886. WILKINS, GEORGE, M.D., 898 Dorchester St., Montreal, Canada.
*1886. WILSON, JAMES C., M.D., 1437 Walnut St., Philadelphia.
*1886. WOOD, HORATIO C., M.D., 1925 Chestnut St., Philadelphia.

CONSTITUTION.

(As Amended May 13, 1890.)

Article I.

Object and Name.

This Association has for its object the advancement of scientific and practical medicine, and shall be known as The Association of American Physicians.

Article II.

Members.

The number of active members shall be limited to one hundred. Physicians of sufficient eminence to merit the distinction may, to a number not exceeding twenty-five, be elected honorary members, and as such shall be entitled to attend all meetings and to take part in the proceedings, but not to vote.

Membership shall lapse by reason of absence from three successive annual meetings without reason given acceptable to the Council. An excused absence shall not be regarded as an attendance. Membership may be forfeited for reasons deemed sufficient by the Association.

Article III.

Officers.

The Officers of the Association shall be a President, a Vice-President, a Secretary, a Recorder, a Treasurer—all to be elected annually; five Councillors—one to be elected each year for a term of five years; and a Representative to serve on the Executive Committee of the Congress of American Physicians and Surgeons, to be elected at the annual meeting immediately following the Congress.

Article IV.

Duty of Officers.

The duties of the President, Vice-President, Secretary, and Treasurer shall be those usually assigned to these officers. The Recorder

shall secure the papers read and also proper notes of the discussions thereon, and shall publish the annual volume of Transactions. The five Councillors shall constitute a Committee of Nomination of Officers, and as such shall present a report at the commencement of the morning session of the last day of the annual meeting, at the conclusion of which session the election shall be held by ballot. The Representative on the Executive Committee of the Congress shall have full power to represent the Association on all ordinary questions, but must be authorized by the Council of this Association before assenting to the admission of any Society to the Congress.

Article V.

Council.

The officers of the Association shall constitute the Council, of which four members shall constitute a quorum. It shall be the duty of the Council to supervise the affairs of the Association, to make all the arrangements for the annual meeting, to suggest the subjects for debate, and to consider the nominations for membership and report on them at the meeting at which they shall be balloted on.

Article VI.

Meetings.

1. The Association shall hold an annual meeting in the city of Washington, D. C., at a time designated by the Council.

2. The President shall call the meeting to order and open the session by an address not exceeding half an hour in length. In his absence the Vice-President shall preside, and in the absence of both these officers, the senior Councillor.

3. Then shall follow original communications, discussions on subjects of general interest in the department of medicine and pathology, demonstrations in pathology, and miscellaneous business.

4. Authors of papers, and referees and co-referees who open a discussion shall not occupy more than thirty minutes each; and in the discussion following, the remarks of each speaker shall be limited to ten minutes.

5. The referees, co-referees, and authors of papers shall send

abstracts of their papers to the Council for distribution to members previous to the meeting.

Article VII.

Quorum.

Any number of members present at the appointed time of the annual meeting shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for altering the Constitution, twenty-five members shall be necessary.

Article VIII.

Election of Members.

Nominations to membership, signed by two members who are not officers of the Association, must be made in writing at an annual meeting of the Association; and within six months of the time of nomination the nominators shall transmit to the Council letters stating the qualifications of the nominee and also a list of his professional positions and publications. The Council shall report those nominations which are approved by it, to the next annual meeting for action. An affirmative vote of three-fourths of the members present shall be necessary for the election of active members, but for the election of honorary members an unanimous vote of those present shall be required.

Article IX.

Annual Dues.

The annual dues of the Association shall be fifteen dollars, from the payment of which honorary members shall be exempt.

Article X.

Amendments to Constitution.

Amendments to the Constitution must be proposed in writing by five members at an annual meeting and must be acted upon at the succeeding annual meeting, the notices for which shall contain an announcement of the proposed amendments; and such amendments shall require for their adoption an affirmative vote of three-fourths of those present.

MINUTES

OF THE

SIXTH ANNUAL MEETING,

Held in the Grand Army Building, Washington, D. C., September 22, 23, 24, *and* 25, 1891.

The following members were present:

From New York: Drs. Charles L. Dana, Francis Delafield, A. Jacobi, Francis P. Kinnicutt, Alfred L. Loomis, William T. Lusk, George L. Peabody, T. Mitchell Prudden, Beverley Robinson, J. West Roosevelt, A. A. Smith, W. Gilman Thompson.

From Philadelphia: Drs. J. M. DaCosta, J. P. Crozer Griffith, Hobart A. Hare, I. Minis Hays, Morris J. Lewis, S. Weir Mitchell, John H. Musser, William Pepper, Wharton Sinkler, Horatio C. Wood.

From Baltimore: Drs. I. E. Atkinson, Samuel C. Chew, W. T. Councilman, Frank Donaldson, Henry Mills Hurd, Thomas S. Latimer, F. T. Miles, William Osler, William H. Welch.

From Washington: Drs. John S. Billings, Samuel C. Busey, Robert T. Edes, W. W. Johnston, D. W. Prentiss.

From Boston: Drs. Reginald H. Fitz, James J. Putnam, Frederick C. Shattuck, George B. Shattuck.

From Albany: Drs. Henry Hun, Samuel B. Ward.

From Ann Arbor: Drs. Heneage Gibbes, Victor C. Vaughan.

From Buffalo: Drs. Charles Carey, Charles G. Stockton.

From Aiken, S. C.: Dr. W. H. Geddings.

From Cambridge: Dr. Henry P. Walcott.

From Chattanooga: Dr. James E. Reeves.

From Chicago: Dr. I. N. Danforth.

From Cincinnati: Drs. F. Forchheimer, James T. Whittaker.
From Denver: Dr. Samuel A. Fisk.
From Jamaica Plain: Dr. Harold C. Ernst.
From Montreal: Dr. James Stewart.
From Pottsville: Dr. John T. Carpenter.
From Richmond, Ind.: Dr. Charles S. Bond.
From St. Louis: Dr. G. Baumgarten.
From Toronto: Dr. J. E. Graham.

Session of Tuesday, September 22d.

President Pepper called the Association to order at 10.20 A.M, and delivered the following

OPENING ADDRESS.

To those who share the feelings of close relationship which the earnest and friendly meetings of our Association have fostered among us, it will not seem strange that I pause, before proceeding to our scientific work, to speak of our fellow-members who have been taken from us during the past year.

Hosmer Allen Johnson, a founder, trustee, and professor of the Chicago Medical College, and one of our original members, died February 26, 1891, at the age of sixty-eight years. In the truest sense of the words, he was an ornament to our profession. Dignity and elevation of character, blended with rare charm of presence, conferred additional distinction upon his high scientific and literary attainments. His memory will be cherished not only in the city of his adoption, but by all who had the privilege of his friendship.

James Kingsley Thacher, Professor of Physiology in the Medical Department of Yale University, and an original member of our Association, died on April 20, 1891, at the age of forty-four years. Descended from a line of ancestors eminent for vigor and originality of intellect, Dr. Thacher early displayed rare powers as an investigator and thinker. It was not until the age of thirty-three, and after he had won international distinction by his researches in comparative anatomy and physiology, that he began the practice of medicine. He rapidly attained the front rank of the profession, and during the remaining years of his life his frequent contributions to medical literature were

of exceptional value as embodying the work of a highly trained scientist dealing with problems of practical medicine. It is difficult to overestimate the loss sustained in the early death of one who so early illustrated the highest type of the physician—the student of Nature as revealed in the functions and disorders of the human body.

RICHARD LEA MACDONNELL, Professor of Clinical Medicine in McGill University, had been a member of our Association but a short time when his death occurred on July 31, 1891, at the sadly early age of thirty-five years. He possessed gifts and ability of high order as clinician, as writer, and as teacher. He had already accomplished much valuable work, and was so well equipped in purpose, powers, and position that a brilliant career was confidently expected. The Association has lost in him one of its most promising members.

Out of our short list of Honorary Members, Fordyce Barker and Joseph Leidy have gone. DR. BARKER died May 30, 1891, at the age of seventy-three. His long life seemed all too short for the countless acts of courtesy and charity which he found place for in a career rich in professional and social success. The delightful charm of the man almost threw into shade the remarkable gifts of the physician. His tact and urbanity were perfect, and his hospitality boundless, so that he was the paragon of hosts. The affectionate solicitude with which he lavished on his patients, rich and poor alike, the resources of his skill, made him one of the most successful and beloved of physicians. His large-hearted sympathy and benevolence made him eager in the organization and service of all movements for the relief of suffering and the elevation of his fellows. The rich treasures of his experience and his strict scientific integrity made his publications valued in all parts of the world. These many honorable distinctions made it eminently proper he should be placed on the list of our Honorary Members, and in his death we all have to lament the loss of a dear friend and a cherished colleague.

In the death of JOSEPH LEIDY, which occurred on April 30, 1891, at the age of sixty-eight years, the medical profession in America lost its most loved and honored member, and American science its most illustrious representative. It makes a difference to the world when such a man passes away. At his birth Nature gave him her accolade, and all his life long he was loyal to the holy quest of truth, which is the vow imposed on those whom she invests as her chosen knights.

Who can say how much of the marvellous and inexhaustible knowledge of Nature this great man possessed came from the singleness of his life and the purity of his heart? Who can say how many of the miserable shortcomings we all exhibit even in our best work, spring from the selfishness and the prejudice we allow to mix with it? Leidy never had a theory to support or a purpose to serve. The all-sufficing motive of his life was to learn the truth of Nature and to help others to learn it also. To the last he kept the humility and the simplicity of a little child. No delight could surpass what he felt when new facts were disclosed to him, unless it were that with which he would share with others all he knew. He made great discoveries in various fields of scientific research; but he never seemed to feel any credit was due to him. It merely was that he had chanced first to see that particular fact. It was no achievement of his. Nature had but given him one more little glimpse of her truth. He looked at all natural things with the same fresh, clear-eyed directness. It did not matter by whom, or under what names, or in what surroundings an object was brought before him; he simply saw the thing itself. In this way he detected blunders innumerable, and became a general referee to whom all sorts of supposed remarkable discoveries were submitted. The certainty with which he could detect the real nature of the object, and the simple, genial way in which he would explain it, made irritation impossible. All knew he would treat an inaccurate observation of his own in the same kindly but unsparing fashion.

If only the facts were discovered, it mattered not to him by whom the discovery was made; and windy battles over claims of priority or selfish struggles to preëmpt fields of investigation were alike impossible to him. More than once he turned aside from lines of research in which he was the pioneer, and where brilliant discoveries were in sight, as soon as he found there were others who longed to win distinction in the same field. I could never see that he enjoyed their triumphs any less than if he himself had won them.

Incapable himself of jealousy, or untruth, or disloyalty, he seemed also incapable of thinking evil of others. In all matters of business he would have been readily imposed upon, and his confidence was freely bestowed on all who sought it. But in the estimation of the scientific value of a man's work he was in many lines of research the very highest and the most candid authority.

Of course, he had no enemies. All were united in respect and affection for him. But only those who lived in close and frequent intercourse with him can tell what elevating and humanizing influences this man of science diffused around him. It helped you to be truthful, simple, and liberal merely to meet him and talk with him. I think few men have been more loved by men than he was; and I know not if there be a higher tribute than this to a man's nature. I shall not attempt to tell what Leidy achieved in many branches of science. The mere fact that his scientific contributions numbered fully eight hundred conveys little idea of the range of subjects they covered, the epoch-making character many of them possessed, or the enormous amount of patient labor bestowed on the thousands of exquisite illustrations they contained. I cannot tell you what he was to his colleagues or to his students in the University of Pennsylvania, where for thirty-eight years he filled the Chair of Anatomy. I feel sure that every colleague in the faculty and every student in the college during that long time was influenced for good by contact with this pure and lovable man. For to Leidy the ever-growing fulness of knowledge brought increasing humility and wonder at the boundless mystery of Nature. And as the close of a profound study of one after another field of natural history added to his sense of the inadequacy of our powers to cope with the problems of creation and life, his feeling of the necessity of a God of Nature strengthened and deepened. Only a few days before his death, as I stood by his bedside, he chanced to notice the flowered pattern of the carpet on the chamber floor, and said: "How can they work flowers in a carpet? We love flowers! No one would tread on flowers!" And with his heart full of such gentle thoughts he lapsed into peaceful unconsciousness—like a tired child falling asleep in the bosom of the Nature he had loved so long and so well.

It would seem to me an abuse of a rare privilege were I to add to what I have said more than a few but cordial words of welcome. In thanking my colleagues, the members of the Association of American Physicians, for the honor conferred upon me when called to preside over this meeting, I may couple with these thanks a no less hearty congratulation that the recurrence of our Congress year finds our Association not only instinct with life, and in close touch with what is best and most progressive in medical work, but establishes

the fact that participation in the Congress certainly does not detract from the interest and importance of our own meeting.

No less may I join with our warm and brotherly greeting to the distinguished guests who have accepted our invitation and honor us with their presence, the gratifying claim that the many charms of a visit to this country, and the great pleasure to be given and received in the kindly social intercourse of this week, have not been more potent attractions than the prospect of sharing in the rich programme of scientific work arranged for this Association and for the Congress.

So far at least as medical men are concerned, one need no longer repeat the assurance that when they cross the ocean they change not their feelings but only their horizon. There exists no barrier to our intercourse. The complete solidarity of our science o'ertops all divisions of race or place. The progress and the interpenetration of knowledge first outgrew personal authority, and have now outgrown the limits of national schools of science.

The existence of this society of clinicians and pathologists is by no means a protest against specialism in medical science. Its presence here in this Congress is typical of the present attitude of scientific medicine to specialism. Just as this great meeting would be crippled without the participation of many special societies, so would our own membership be sadly incomplete did it not include many eminent specialists. General medicine and general surgery to-day are federations of specialties, and the general clinician, even of the broadest gauge, in dealing with obscure and complicated cases acts but as the leading partner in a medical firm.

This is the natural and desirable development of our professional relations. The courts where the issues of our causes are decided are open constantly, and have unlimited jurisdiction. The microscope, the ophthalmoscope, the hæmatometer, the tests of organic chemistry, are witnesses whose presence is always available, and whose testimony as to matters of fact is unimpeachable. No cumbrous accumulation of papers and elaborate machinery of procedure hamper our legislation. In the privacy of two or three consulting-rooms are determined with all reasonable certainty and celerity the issue of causes vastly more vital to the parties interested, and scarcely less so to the community at large, than those which fill columns in the daily press and block the slow wheels of litigation for years. Remedial measures are agreed

upon and carried into effect which require such masterful decision, fertility of resource, and energy of action as stamp the great leaders in all the hard-fought battles of the world.

It is a supreme glory of our service that it is restricted to no nation, no dynasty, no place, no class. The monarch of the mightiest empire and the poorest patient in the hospital ward command and receive the same efforts in their behalf.

It is by the combination of the highest specialism, wrought by mutual trust and trained coöperation into absolute unity, that the great triumphs of medicine and surgery are now achieved. The evident truth of this is the basis of the work of our Association. The broadening field, the increasing precision of our work, the vast scope of the questions of heredity, of climatic and racial influence, of hygiene and dietetics, of mental and moral regimen—of all that is included in preventive medicine, the great battlefield of the future, and which must be used as far as understood in the struggles of the remedial medicine of to-day, call for a coöperation—not local, but national and international—which shall bring into closer touch, better mutual knowledge, and deeper mutual trust, all earnest workers in scientific medicine.

It is, then, with the happy assurance that our work here is in line with the great onward movement of the day, that I announce the opening of the sixth annual session of the Association of American Physicians.

The Treasurer, Dr. Johnston, read his annual report, which was referred to an Auditing Committee consisting of Drs. Hays and Wood.

On recommendation of the Council Drs. Andrew H. Smith and Wm. P. Northrup, of New York, Dr. A. L. Mason, of Boston, and Dr. A. McPhedran, of Montreal, were unanimously elected members of the Association.

Dr. Kinnicutt, of New York, Dr. Ernst, of Boston, Dr. Osler, of Baltimore, and Dr. Griffith, of Philadelphia, presented reports on "The Treatment of Visceral Tuberculosis by Koch's Method," which were not further discussed.

In the absence of Dr. Bridge, his paper on "The Climate of Southern California for Respiratory Diseases" was read by title.

Dr. Roosevelt, of New York, read a paper on "Experimental Studies on the Causes of the Localization of Pulmonary Phthisis and

Certain Other Infectious Diseases in the Lungs," which was discussed by Drs. Welch, Ord, Jacobi, Vaughan, Shattuck, and Roosevelt.

Dr. W. T. Gairdner, Professor of Medicine in the University of Glasgow, read a paper entitled "An Experiment in Sanitary Administration—Cholera in Glasgow, 1866," which was not discussed.

Adjourned at 1.30 P.M.

Session of Wednesday, September 23d.

President Pepper called the Association to order at 10.15 A.M. The discussion on the "Remote Results of the Removal of the Ovaries and Tubes" was opened by Drs. Lusk, of New York, and Sinkler, of Philadelphia, and was continued by Drs. Putnam, Mitchell, Gairdner (Glasgow), Lee (New York), Wathen (Louisville), and Lusk.

Dr. Stewart read a paper on "Nerve-stretching in Inveterate Cases of Trigeminal Neuralgia," which was not discussed.

Dr. Delafield read a paper "On the Diseases of the Kidneys Popularly Called Bright's Disease," which was discussed by Drs. Andrew H. Smith, Gairdner (Glasgow), Councilman, Vaughan, Griffith, and Smith.

The reading of the papers of Drs. Tyson and Atkinson was postponed.

Adjourned at 1.30 P.M.

Session of Thursday, September 24th.

President Pepper called the Association to order at 10.15 A.M.

The discussion on "The Relations between Arterial Disease and Visceral Changes" was opened by Drs. Peabody and Councilman, and was continued by Drs. Ord (London), Gairdner (Glasgow), and Councilman.

Dr. Fitz read a paper on "Intestinal Perforation in Typhoid Fever," which was discussed by Dr. DaCosta.

Dr. Walcott read a paper on "The Relation of Drinking-water to Disease," which for lack of time was not discussed.

Dr. Griffith read "A Contribution to the Pathology of Pernicious Anæmia," which for lack of time was not discussed.

The reading of the paper of Dr. Theobald Smith was postponed.

Adjourned at 1.30 P.M.

Session of Friday, September 25th.

President Pepper called the meeting to order at 10.15 A.M.

Dr. Billings read a paper on "The Conditions and Prospects of the Library of the Surgeon-General's Office and Its Index-Catalogue," which was discussed by Dr. Gairdner (Glasgow).

Dr. Prentiss reported the "Sequel to a Case of Slow Pulse," and the report of the autopsy was made by Dr. Edes, which paper was discussed by Dr. Welch.

Dr. Prentiss exhibited specimens showing the effect of pilocarpine in changing the hair from a light blonde color to dark black.

Dr. Pepper called the attention of the members to the question of the desirability of widening the membership of the Association by the addition of men who are eminent workers in the domain of hygiene and of the etiology of disease but who are not physicians; and this proposition was favorably discussed by Drs. Billings and Busey, and on motion of the latter the matter was referred to the Council with the instruction to introduce an amendment to the constitution if necessary to cover these cases, which amendment should be acted upon at the next meeting of the Association.

Dr. Theobald Smith read, by invitation, a paper on "Changes in the Red Blood-corpuscles in the Pernicious Anæmia of Texas Cattle Fever," which was discussed by Drs. Welch and Smith.

Dr. Musser read a paper on "Grave Forms of Purpura Hæmorrhagica," which was discussed by Drs. Welch, Pepper, Prentiss, and Graham.

Dr. Atkinson read a paper on "Bradycardia in Acute Articular Rheumatism," which was discussed by Drs. Pepper, H. P. Bowditch (Boston), Ord (London), and Atkinson.

The Auditing Committee, Drs. Hays and Wood, reported that they had examined the Treasurer's report and found it correct.

The Association then proceeded to the election of officers and unanimously elected the following officers for the ensuing year:

President.—Henry M. Lyman, of Chicago.
Vice-President.—George Ross, of Montreal.
Secretary.—Henry Hun, of Albany.
Treasurer.—W. W. Johnston, of Washington.
Recorder.—I. Minis Hays, of Philadelphia.

Adjourned at 1 P.M.

Henry Hun, *Secretary.*

PAPERS

READ AT THE

SIXTH ANNUAL MEETING

OF THE

ASSOCIATION OF AMERICAN PHYSICIANS,

HELD AT

WASHINGTON, D. C.,

SEPTEMBER 22, 23, 24, AND 25, 1891.

NOTICE.

THE Association assumes no responsibility for the statements and opinions expressed in the papers read at its meetings.

TREATMENT OF VISCERAL TUBERCULOSIS BY KOCH'S METHOD.

By FRANCIS P. KINNICUTT, M.D.,
PHYSICIAN TO ST. LUKE'S HOSPITAL, NEW YORK.

During the interval between December 10th and June 1st, forty-two patients suffering from various forms of tuberculous disease were inoculated with Koch's fluid, under my personal supervision, in the wards of St. Luke's Hospital. The list embraced thirteen cases of pulmonary tuberculosis, in seven of which evidence of laryngeal tuberculous disease of varying degrees of severity also existed, six cases of well-marked lupus, five cases of joint tuberculosis, four cases of tuberculous adenitis, two cases of bone tuberculosis, two cases of tuberculous prostatitis, one case of tuberculous epididymitis, one case of rodent ulcer, and eight cases inoculated for the purpose of diagnosis.

The discussion being limited by announcement to the treatment of visceral tuberculosis, the present paper will be confined to a consideration of the results obtained in the cases of pulmonary and laryngeal tuberculous disease. The report is necessarily incomplete, as the limit of time imposed upon all papers read before the Association precludes the recital of many details. The continuous histories are given to May 15th. During the latter two weeks of that month, eight of the nine phthisical patients remaining in the hospital were sent into the country, several to institutions for consumptives, that they might have the benefit of a more favorable environment than that afforded by a city hospital during the months of summer heat. One patient insisted upon going to her own home in the city, where her environment was particularly unfavorable. The histories of these patients subsequent to May 15th, in so far as it has been possible to obtain any report from them, will be given in an appendix.

The only point in the technique of the treatment to which I shall refer, is the desirability of making use of freshly prepared solutions of the fluid. Judging not only from Koch's original statement, but from the reports of various observers, the carbolic acid solutions apparently deteriorate in efficacy by keeping. In my wards, all inoculations were given at a specified hour each day, and the solution was prepared from the original fluid at this time. The rule in treatment was not to exceed one milligramme for the initial inoculation in adults in any case, and not infrequently only a half milligramme was given. In the cases of pulmonary tuberculosis, in the earlier period of inoculations, the severity and duration of the general rather than the local reaction, provided the latter was not too acute, was a guide to the frequency of reinoculations. A little later it was deemed advisable to pursue a different course. The subsidence of the physical signs of local reaction, when present, was awaited and the strength of the dosage was only very gradually increased. The general condition of the patient was also carefully considered; idiosyncrasies were studied; where the vitality was markedly lowered by the disease or was apparently unfavorably affected by the inoculations, they were only repeated at comparatively long intervals. An interval of a week, and even of two weeks, was sometimes permitted to elapse between the inoculations.

Whether the effect of the fluid is to produce a necrosis of tuberculous tissue proper, or to excite an acute inflammatory process in the immediately contiguous tissues which might beneficially lead to the extrusion of the former, as Virchow is inclined to believe, such a course as I have outlined seemed the most rational and has apparently been justified by continued clinical experience. *Gradual* destruction, separation and elimination, or encapsulation, is the course pursued by Nature in her attempt toward repair in pulmonary tuberculosis, and it is reasonable to expect that the best results should be obtained by imitating such a course as nearly as possible. A similar method of treatment was pursued in the cases of joint and bone tuberculosis, especially where sinuses were absent. Patients suffering from lupus were treated respectively by inoculations frequently repeated and rapidly increased in strength, and by inoculations only given after the almost complete subsidence of local reaction. The different methods in these cases were attended with very similar results.

The thirteen cases of pulmonary tuberculosis are divided for convenience into groups.

A. *Cases in which notable improvement in the pulmonary and general condition occurred.*

B. *Cases in which either no improvement occurred or improvements in certain respects was observed and not in others.*

C. *Cases in which distinct deterioration in the condition of the patient or progress of the disease accompanied the inoculations.*

GROUP A.—Five cases are embraced in the *first group*. The ages of the patients varied from seventeen to forty-two years. There was a history of family predisposition in three of the cases. The duration of the disease in two cases was nine months and a year respectively, in three the history was unsatisfactory in regard to this point. In all there had been progressive loss of strength and flesh. In two cases severe hæmoptyses had occurred ten days and two weeks previous to admission. In none was there a history of night-sweats. The sputa were abundant in four of the cases and contained bacilli in large numbers; in one, the daily amount of sputum was no more than a half ounce, and careful examination by Dr. Prudden failed to detect the presence of bacilli, *before* inoculation. The physical signs in four indicated infiltration of the apex of one lung; in one of these rather abundant subcrepitation existed over the affected area; in a second, scanty, dry crepitation was appreciable immediately beneath the clavicle; in the remaining two, adventitious sounds were absent. In the fifth case, there was evidence of an apparently plastic exudation involving the lower half of the posterior and axillary pleura of the left side, with retraction of the chest wall and doubtful signs of disease at the apex of the same lung. In two of the cases there was a slight evening rise of temperature previous to inoculation; in three the temperature was normal.

The larynx was involved in only one case, and in the form of moderate infiltration, without ulceration. Three of the above cases were discharged from hospital after eleven, thirteen and sixteen weeks of treatment, having received 0.016 gramme, 0.019 gramme, and 0.021 gramme, as the maximum single inoculation.

Constitutional reaction, as indicated by the temperature, followed inoculations of 0.003 gramme, 0.001 gramme and 0.002 gramme, and ceased to be developed after inoculations of 0.011 gramme, 0.012

gramme, and 0.013 gramme, corresponding to the above order. The gain in weight was four pounds in two cases, eleven pounds in one. The sputum in one case amounted to half an ounce, in two to nine drachms, on admission; it was increased in all during the earlier inoculations, and gradually diminished in amount later. Both sputum and cough were practically absent on discharge, and the temperature was normal throughout the twenty-four hours.

The bacilli in the sputum of one were enormously increased in number; in one, not materially affected during the earlier period of treatment; and in the case in which they were not detected *previously* they were found in considerable numbers *after* the first inoculation. In all, they gradually diminished in number, and before discharge in several of the many examinations, though not consecutively, they were absent. The examinations were kindly made by Dr. Prudden, the number of bacilli in the total sputum for the twenty-four hours being estimated. Inasmuch as the tubercle bacilli are very unevenly distributed in the sputum, only a very indefinite idea of the number present can be obtained by the examination of even those portions in which experience has shown they are most commonly present.

To accurately observe the effect of a special mode of treatment upon the elimination of bacilli in the sputum, Dr. Prudden adopted the following procedure: The sputum for the twenty-four hours was mixed with a saturated solution of borax in water, placed in a large jar, and allowed to stand for twenty-four or forty-eight hours, the jar being frequently vigorously shaken to assure an intimate admixture of its contents. At the end of this time the mixture was usually homogeneous, and accurately measured portions were taken for examination. The common unit taken by Dr. Prudden was one cubic centimetre.

It should be borne in mind in examining the tables, of which three, as examples out of many from each group, have been selected and appended, that an apparently very large number of bacilli recorded as being present in one cubic centimetre represents a comparatively small number in a cover-glass; for example, 400,000 bacilli in one cubic centimetre represent 800 bacilli in a cover-glass in which forty fields, the number regularly examined by Dr. Prudden, are counted. Again, 500 bacilli in a cubic centimetre represent 1 bacillus in an entire cover-glass.

In two of the cases the pulmonary physical signs improved in the following respects: The impairment in resonance notably diminished, and the character of the respiratory murmur became very nearly normal, although occasional fine, dry crepitation after cough was still appreciable immediately beneath the clavicle in one case. In the third case, the pleuritic signs previously mentioned remained very similar to those noted on admission. The lesion of the pulmonary tissue proper in this case was difficult to localize, on account of the involvement of the pleura. The two remaining cases are still in the hospital (May 1st), after two and four months of treatment. In one, the laryngeal infiltration has undergone no appreciable change during treatment. The gain in weight has been eight and a half pounds in the case longest under treatment, four and a half pounds in the other. The pulmonary physical signs have shown quite as marked improvement, and in the same respects, as in the cases above recorded. In one, the abundant subcrepitation heard immediately beneath the clavicle on admission has disappeared, and only occasional dry crepitation is now heard. The temperature in both is normal throughout the twenty-four hours. In both, the general appearance and condition have greatly improved. The bacilli in one case continue to be found in large numbers in the sputum; in one they have very notably diminished (from 342 in a cover-glass, the average of many examinations, to 10). No hæmoptysis occurred at any time during treatment in any of the five cases, although it will be recalled that copious pulmonary hemorrhages had been present in two of the cases immediately before admission. In considering the improvement in the physical signs, the suggestion must be borne in mind that a diminution in dulness and a more normal character of the respiratory murmur may proceed from the "disappearance of *intra-alveolar exudation*, and not from the destruction of *inter-alveolar tuberculous tissue*, the two prominent factors in pulmonary tuberculosis."

The improvement in the five cases which have been narrated is certainly very notable—more so than I have personally seen in a similar number in a corresponding stage of the disease, treated by other methods in hospital for a similar period of time. It should be stated that these patients received cod-liver oil or creasote, or both, during a greater portion of the period of inoculation; on the other hand, that such a medication had been used by all previous to inoculation, and without

apparent benefit. One of the above number had been under my personal observation and treatment for a year.

GROUP B.—Four cases comprise this group. Two of the cases present points of interest in connection with the laryngeal lesions present.

CASE I. presented the physical signs, on admission, of infiltration of the upper third of the upper lobe of one lung. Abundant subcrepitation was present over the supra- and infra-clavicular regions, and scantily over the upper portion of the scapular region. The sputum contained numerous tubercle bacilli. There was a negative history of hæmoptysis and night-sweats. There was a slight afternoon rise of temperature before inoculation. Reaction followed the inoculation of 0.0005 gramme. Nine inoculations only have been given during two months of treatment, the largest single inoculation being 0.005 gramme. Reaction continues to be developed. At present, in the intervals between the inoculations, the maximum afternoon temperature does not exceed 100°, and is often normal. The gain in weight has been ten and a half pounds. The physical signs show improvement in the disappearance of all adventitious sounds over the scapular region, and in a diminution in the amount of subcrepitation heard anteriorly. The impairment of resonance remains unchanged. Numerous bacilli are still found in the sputum.

CASE II.—Physical signs of infiltration of considerable areas in the upper lobe of the left lung, without evidence of excavation, and of thickening of the entire pleura of the same lung, were present on admission. The temperature for a month previous to inoculation, while the patient was under observation in the hospital, was irregular, with an occasional maximum evening rise to 102°. There had been very numerous hæmoptyses previous to admission, and two occurred in hospital (one of eighteen ounces) before inoculation. Laryngoscopic examination showed general infiltration of the posterior portions of the larynx and posterior commissure, especially of the left side. There was an ulcer over the left processus vocalis, extending into the posterior commissure. The sputum contained numerous bacilli. Reaction followed the second inoculation of 0.002 gramme. Thirty-two inoculations have been given during a period of five months, of a maximum strength of 0.021 gramme. The ulceration in the larynx increased for a time, but within the last three weeks improvement has been noted.

At the present date the pulmonary physical signs show improvement in the following respects: Crepitation over the affected areas is exceedingly scanty, is very fine and dry in character, and is only heard after cough. The percussion note is practically of the same quality as on admission. The temperature, however, is normal throughout the twenty-four hours (constitutional tolerance to the tuberculin was established after the twenty-third inoculation of 0.013 gramme), and there is a gain in weight of six pounds. The disappearance of fever, the improvement in the physical signs and in

the patient's general condition, point to a cessation in the previous *activity* of the pulmonary disease. The sputum has diminished from three ounces in the twenty-four hours to less than a drachm, but still contains rather numerous bacilli.

Laryngoscopic examination shows a diminution in the infiltration, and the existence of ulceration is noted by Dr. Lefferts in his diagram as doubtful. As the only process of cure in laryngeal tuberculosis—*i. e.*, in tuberculous disease of mucous membranes—consists in the breaking down of the tuberculous tissue into an ulcer and the ultimate cicatrization of the latter, the distinct increase in the lesion for a period may perhaps justly be regarded as a step toward repair. No hæmoptysis occurred in the above case *after* inoculation.

CASE III.—There was evidence before inoculation of slight infiltration at the apex of the left lung. Scanty crepitation was present over the supraspinous fossa, but was absent anteriorly. For three weeks previous to inoculation, while in hospital, there was an irregular but constant rise of temperature in the afternoon, the maximum being 102°. The weight remained the same during this period. The sputum was copious, and contained numerous bacilli. There was a negative history of hæmoptysis and night-sweats. Laryngoscopic examination showed erosion of the right vocal cord, ulceration in the inter-arytenoidal commissure and infiltration over the left arytenoid.

Reaction followed an inoculation of 0.001 gramme. Of all the pulmonary cases inoculated, the present one showed the least constitutional tolerance to the fluid. Notwithstanding the apparently slight lesion of the lung and the not very severe degree of laryngeal disease, inoculations for many weeks were accompanied with much constitutional disturbance aside from the elevation of temperature. Exceptional caution was necessitated in increasing the dose and in regulating the interval between the inoculations. After the first two weeks of treatment the cough markedly diminished, and the sputa from amounting to two ounces on admission gradually fell to one to two drachms in the twenty-four hours, and the bacilli diminished from 650 in a cover-glass (40 fields) to 120, the above numbers being the average of many examinations. The afternoon rise of temperature was less, often being a fraction below 100°, and on February 16th the patient's weight was twelve pounds in excess of that immediately before the first inoculation.

It was impossible to *detect any difference in the physical signs between the two apices.* Little appreciable change was noted in the laryngeal lesion. From this date up to the present time, although the same absence of pulmonary physical signs exists, the disease in the larynx has made notable progress, the sputa have proportionately increased in amount, the bacilli numbered 800 in a cover-glass at the last examination, and the patient has lost five pounds in weight. The temperature curve has again become more irregular and exhibits a higher range.

Laryngoscopic examination on April 2d showed a general increase in the

infiltration previously existent, and new infiltration over the *right* arytenoid and a distinct increase in the area of the ulceration. On April 28th an ulcer of the right vocal cord was appreciable, and the ulceration in the inter-arytenoidal commissure was more extensive and deeper. Influenced by the observations made in the previous case, the inoculations have been continued. The patient has been under treatment for four months.

CASE IV. was apparently one of bilateral tuberculous pleurisy without effusion, with an accompanying lesion of the pulmonary tissue of one lung. The physical signs during reaction were of much interest, but they are very similar to-day to those noted on admission. The patient is still under treatment.

GROUP C consists of four cases.

CASE I. had mitral and advanced renal disease on admission, in addition to infiltration at one apex. Scanty dry crepitation was also present over the anterior mediastinum. Reaction followed the second inoculation of 0.002 gramme. The albumin in the urine directly increased in amount, red blood-discs appeared, and hyaline and granular casts were found in larger numbers. Following the fourth inoculation of 0.0025 gramme headache and vomiting were developed; the latter symptom was controlled only with difficulty. The amount of urinary albumin increased to 4 per cent. from 1 per cent. (volumetric estimation) on admission; the urine presented a smoky hue from the presence of blood-discs and their coloring matter, and contained still more numerous casts. The physical signs of a mediastino- or pleuro-pericarditis were appreciable. The signs at the apex remained unchanged. Inoculations were discontinued, and gradually all the above symptoms and signs declined to the point noted on admission.

CASE II.—Physical signs were present on admission of areas of infiltration throughout the upper lobe of one lung and of slight consolidation at the apex of the other. Evidence of actual excavation was wanting, although disintegration was apparently proceeding in localized areas.

Laryngoscopic examination showed infiltration in the inter-arytenoidal commissure. The right vocal cord was invisible through the overhanging, swollen ventricular bands. The left cord was simply hyperæmic. The temperature was practically normal for the twenty-four hours preceding inoculation. A sharp general reaction followed the first inoculation of 0.0005 gramme; it was accompanied by a slight epistaxis. Following the fifth inoculation of 0.002 gramme slight pain was complained of in the right iliac fossa, and there was a little tenderness and sense of resistance in this region. These symptoms speedily disappeared on poulticing. The twelfth inoculation of February 8th of 0.004 gramme was followed by all the symptoms and signs of an appendicitis (local peritonitis, tumor in the inguinal fossa, etc.). Epistaxis and hæmoptysis also occurred. Frequently recurring pulmonary hemorrhages, rather profuse in character, were present for the subsequent ten days. The patient was kept under the influence of morphine, and poultices

were continuously applied over the inguinal region. The signs of appendicitis gradually disappeared and hæmoptysis ceased. Inoculations were discontinued after the twelfth. From February 8th to February 21st there was an irregular temperature curve. From this date it gradually declined, and for the past month it practically has been normal. Within the past few days there has been a recurrence of the appendicitis, the signs of which are again disappearing. The pulmonary physical signs at the present date are very similar to those on admission.

Very early in the period of inoculations the swelling of the ventricular bands disappeared, revealing a small ulcer of the right vocal cord. This gradually disappeared. The infiltration in the inter-arytenoid commissure remained unchanged. On April 2d, seven weeks after the *discontinuance* of inoculations, marked increase in the infiltration and ulceration in its central point was noted. On April 28th the ulceration had appreciably extended. The occurrence of an appendicitis during the period of treatment suggests its possible origin in a tuberculous ulcer.

CASE III.—The only pulmonary physical signs appreciable on admission pointed to a very slight infiltration at the left apex. The evidence of laryngeal disease was considered doubtful. A slight afternoon rise of temperature was noted for the three days the patient was in the hospital prior to inoculation. Bacilli were present in the sputum. Reaction followed an inoculation of 0.001 gramme, and a marked change in the physical signs was at once apparent. It consisted in the development of abundant moist crepitation over the first and second interspaces and in the supra-clavicular region, with distinctly diminished resonance over the same areas. Similar signs were developed in many cases, following the early inoculations, to disappear again on the continuance of the treatment, and were undoubtedly due to transitory local hyperæmia and swelling. The above symptoms, however, did not disappear in the present instance, neither did they materially increase for several weeks, but gradually rubbing and creaking sounds were heard over the scapular region of the same side, indicating an involvement of the pleura, and a small area of fine moist crepitation was noted over the scapular region of the opposite side.

In view of the above conditions and an apparent lack of vitality in the patient noticeable from the first, although the temperature rarely exceeded $99\frac{2}{5}°$ in the intervals between the inoculations, and there was a slight gain in weight (one and a half pounds) up to February 5th, one month after the institution of the treatment, no inoculations were given after that date. They had been twelve in number, with a maximum strength of only 0.002 gramme.

Frequent physical examinations continued to be made with the following results: The impaired resonance in the first two interspaces gradually became marked dulness, and extended over the entire anterior lung area, and abundant moist crepitation was appreciable over the whole of the same. Excavation at points followed, and on April 5th there were the physical signs of two small cavities in the infra-clavicular region. The signs posteriorly over both

lungs revealed no further change from those mentioned above. The process of excavation was attended with a slight and irregular rise of temperature. The evidence is indisputable that either a massive catarrhal or caseous hepatization, gradually leading to localized excavation, *followed* inoculations in this case.

Different opinions may possibly be held of the dependence of the morbid process upon the inoculations. This is the only case under my personal observation in which appreciable lesions of this nature have occurred during treatment with tuberculin.

CASE IV.—There was evidence in this case of rather diffuse infiltration of the left lung, with the implication of a small area in the upper lobe of the right, on admission. Subcrepitation was abundant in scattered areas, but physical signs of excavation were absent. There was also moderate infiltration over both arytenoids and of the ary-epiglottic folds. The sputum contained numerous bacilli. There was an irregular temperature curve with an occasional afternoon rise to 102°. Reaction followed an inoculation of 0.0005 gramme. Eighteen inoculations in all were given of a maximum strength of only 0.003 gramme.

There was apparently gradual progress of the pulmonary disease, although no new areas were involved, and the patient lost four pounds in weight during the ten weeks of treatment. No change was appreciable in the laryngeal lesion.

The impressions which I have received from an experience of nearly nine months in the treatment of various forms of tuberculosis with tuberculin, may be summarized as follows.

They embrace a full recognition of its harmful action and its dangers, as well as what my observations lead me to believe its beneficial effects.

General Impressions.

Tuberculin possesses marked elective affinities for tuberculous tissue.

Its value in differential diagnosis is relative, rather than positive.

Tuberculin not only does not produce immunity, but in certain cases apparently predisposes tissues contiguous to the seat of the original disease, as well as more distant structures, to infection.

The fever and general constitutional disturbance produced by tuberculin are not only harmful, but are probably unessential to its remedial action. This clinical impression is strengthened by very recent chemical investigations, which indicate that tuberculin contains not

one, but several, active principles, and that its activity in producing fever and constitutional disturbance is apparently dependent upon contained substances quite distinct from its remedial principles.

Inoculations of minimum strength gradually increased and given at longer intervals than was originally advised, constitute the safest and probably the most efficient method of its use.

Impressions of the Effects of Tuberculin in the Treatment of Pulmonary Tuberculosis.

Its remedial action is apparently restricted to pulmonary disease in its early stage. In such forms of tuberculosis, the most careful study of the individual, of the history and physical signs of the disease previous to inoculation, does not permit an opinion of the probable nature or degree of reactions or of the ultimate effect of treatment in any given case.

The establishment of constitutional tolerance varies greatly in time in different individuals suffering from apparently similar lesions and cannot be accepted as a basis for prognosis.

Local reactions may continue to be developed under treatment, in the entire absence of constitutional effects, as indicated by the temperature curve.

Tuberculin is apparently capable in exceptional cases, even of incipient disease, of exciting pneumonic processes (catarrhal and caseous hepatization) of varying degrees of intensity. Such processes are probably due to the conveyance into other parts of the lung of cheesy material and liberated bacilli.

In cases of localized tuberculous pleurisy, the inflammatory action excited by tuberculin may lead to a general infection of the pleura.

The production of hæmoptysis is comparatively rare.

Its use necessitates the greatest watchfulness and entails much anxiety on the part of the physician.

In conclusion, it is my impression from clinical observation, that the exceptional dangers and often harmful action of tuberculin do not preclude its employment, and that it exercises a distinctly remedial action in a yet undetermined percentage of cases of pulmonary tuberculosis in its early stage, and an ameliorating effect upon many of the symptoms of more advanced disease. The complexity of conditions often present, even in the early stage of the disease, and the

idosyncrasies of tissue reaction in different individuals, are suggested in explanation of the failure of a remedial action in cases apparently similar.

The most recent observations give promise of an enlarged sphere of usefulness in modifications of the original preparation.

The above impressions must be regarded as liable to modification with continued and more extended clinical study. They find expression only after the first enthusiasm excited by Koch's discovery has been succeeded by a general scepticism of its value, and are the impartial outcome of daily and laborious observations extending over a period of many months.

APPENDIX.—*September 1st.* No answers to letters of inquiry have been received from the three patients of GROUP A, who were discharged from the hospital in a condition to pursue their ordinary occupations. The histories of the two remaining patients in this group, who continued to improve up to the date of their discharge, are briefly as follows:

One has steadily gained in strength and weight, and her general condition is excellent.

The fifth patient has been previously referred to, as insisting upon returning to her home in the city where her environment was particularly unfavorable. Very speedily all her symptoms, which had shown marked improvement, recurred, and finally, five weeks after her discharge from the hospital, on being removed to Dr. Trudeau's sanitarium at Saranac Lake, she was found to have a daily rise of temperature and night-sweats, both of which had disappeared under treatment, and troublesome cough. Physical examination showed increased activity of the disease at the old site, the right apex, and a loss of vesicular murmur at the left, which had not been present previously.

Dr. Trudeau, in a recent letter, writes as follows: "For three months the treatment consisted in an out-of-door life, in the use of creasote, etc. At first, Miss D. slightly improved, but soon began to lose ground again." "At the end of the above period, the inoculations were resumed in small doses. She immediately began to gain in weight, her appetite improved, and her cough markedly diminished. This improvement is maintained at the present time."

GROUP B.

CASE I.—The report is insufficient for the expression of an opinion of the patient's present condition.

CASE II.—There is an absence of sputum, night-sweats and fever, and there has been a gain of nine pounds in weight since discharge. The voice is much stronger and the former laryngeal distress is but slightly felt. The patient's general condition is stated as being good, and he has resumed, after an interval of nearly a year, his usual occupation.

CASE III.—The patient has been an inmate of the House of Rest for Consumptives, and the resident physician's (Dr. Rogers) report indicates an apparent gradual increase in the laryngeal lesion.

CASE IV.—The patient's condition is very similar to that on discharge. There has been neither gain nor loss in weight. He has resumed his usual occupation.

GROUP C.

CASE I.—Inoculations were discontinued in hospital on account of the existence of cardiac and renal disease.

CASE II.—Inoculations were discontinued on the occurrence of hæmoptyses and an attack of appendicitis. The patient's condition is very similar to that while under observation. There has been no recurrence of the appendicitis. There has been one hæmoptysis since discharge.

CASE III.—No report has been received.

CASE IV.—The patient died two weeks subsequent to discharge.

CASE I. GROUP A.—*Discharged after Three Months.*

Date.	Amount of sputum.	No. of tubercle bacilli in 1 c.c.	No. of bacilli per cover-glass, 40 fields examined.
Dec. 13, 1890.	65 c.c.	45,000	90.
" 14, "	60 "	1,126	2.25
" 15, "	52 "	10,000	20.
" 18, "	62 "	40,000	80.
" 21, "	75 "	10,000	20.
" 25, "	60 "	50,000	100.
Jan. 5, 1891.	37 "	0	
" 8, "	78 "	0	
" 19, "	50 "	0	

CASE II. GROUP A.—*Discharged after Four Months.*

Date.	Amount of sputum.	No. of tubercle bacilli in 1 c.c.	No. of bacilli per cover-glass, 40 fields examined.
Dec. 13, 1890.	40 c.c.	130,000	260.
" 15, "	30 "	270,000	540.
" 18, "	37 "	580,000	1160.
" 21, "	17.5 "	40,000	80.
" 25, "	10 "	60,000	120.
Jan. 5, 1891.	15 "	10,000	20.
" 8, "	30 "	0	0.
" 12, "	40 "	5,600	11.2
" 19, "	20 "	1,200	2.4
" 26, "	15 "	400	0.8
March 6, "	10 "	572	1.7

CASE III. GROUP B.—*Still under Treatment after Four Months.*

Date.	Amount of sputum.	No. of tubercle bacilli in 1 c.c.	No. of bacilli per cover-glass, 40 fields examined.
Dec. 3, 1890.	30 c.c.	130,000	260.
" 13, "	100 "	270,000	540.
" 15, "	50 "	360,000	720.
" 18, "	40 "	240,000	480.
" 21, "	27 "	260,000	520.
" 25, "	15 "	440,000	880.
Jan. 12, 1891.	52 "	80,000	160.
" 19, "	35 "	150,000	300.
" 26, "	3 "	40,000	80.
Feb. 21, "	13 "	60,000	120.
March 6, "	50 "	80,000	160.
April 27, "	40 "	400,000	800.

"TUBERCULIN AND TUBERCULOSIS."

By HAROLD C. ERNST, M.D.

PHYSICIAN TO OUT-PATIENTS, MASSACHUSETTS GENERAL HOSPITAL; ASSISTANT PROFESSOR OF BACTERIOLOGY IN HARVARD UNIVERSITY.

I AM indebted to the staffs of the Massachusetts General, the City, and the Children's Hospitals in Boston for the facilities I have had for observing the effects of tuberculin used clinically, and to many gentlemen for assistance rendered whilst the work was going on—notably to Dr. Henry Jackson, who has been untiring in the aid given me.

I shall give but a brief summary of such cases as have come under my care and that seem to be proper to mention as furnishing grounds for the conclusions I have reached. I shall omit entirely an account of those that were treated for so short a time as to make it impossible to draw any conclusions from them, or that were used for testing the so-called diagnostic value of the material. It is hardly worth while to spend time upon a detailed description of the cases at present. So much work of this kind has already been published, that a statement of one's present position is all that is needed. Any permanent benefit that may possibly come from the use of the material under consideration will be for the future to show, and of course has not manifested itself as yet, even if it exists.

The grievous part of the whole matter is the too early announcement and application of laboratory results to clinical practice, and the inevitable destruction of confidence in future work of a similar character that will result from the failure of the hopes that were entertained in regard to this material.

I believe it should be said, however, and I am supported in the assertion by at least some of those best fitted to judge, that the failure of "tuberculin" to accomplish what was hoped for from it does not in the least alter the probabilities that furnish guide-posts to the in-

vestigator for the direction of his work; and that it seems as probable now as last year that, by methods that are still to be worked out, there is to be isolated from the cultures of the various bacteria, or from the results of the activity of these cultures, something that will prove destructive to their activity and hurtful action in the human body. Before this can be accomplished there are still many stumbling-blocks to be avoided and many complicated questions to answer. So that the question that is under discussion at present must be regarded as merely the first uncertain step toward something that may be of great benefit to us all.

I have divided the cases that I wish to report into two classes: those that were either affected with internal tuberculosis alone or in which this form of the disease was the more prominent, and those in which the "surgical" form of the disease was the more marked, but in which the pulmonary or other internal tuberculosis may have been present at the same time.

If the actual presence of the bacilli of tuberculosis and their demonstration be required for a positive diagnosis, a number of my cases must be excluded from the list, and I am one of those who would require this demonstration before consenting to a scientific diagnosis of the existence of tuberculosis. But whether the cases I have reported should be thus excluded or no may be seen in the summary, by the fact that in every one in which the bacilli have not been found, and yet in which there was a clinical probability of the disease being tuberculosis, the fact of the absence of the bacilli has been noted.

One of the lessons that it seems to me should be learned by the experience gained in selecting cases for treatment with tuberculin is the necessity we are under of making an earlier diagnosis than is yet usually the case.

The cases that I think it well to speak of here are as follows:[1]

CASE I.—*Pulmonary tuberculosis of a year's standing. Under treatment for ten weeks.*

Summary.—Number of injections 16; amount used 41.0 mgms.; highest dose 4.5 mgms.; highest temperature 104.4°, after the 7th injection of 2 mgms.

Not relieved.

[1] Further details in regard to any of the cases may be found in the Boston Medical and Surgical Journal, July 2 to August 6, 1891.

CASE II.—*Pulmonary tuberculosis of a year's standing. Under treatment for nine weeks.*

Summary.—Number of injections 33; amount used 252.8 mgms.; highest dose 16 mgms.; highest temperature 103.6°, after the 33d injection of 4.8 mgms. For a time the patient gained weight, and the bacilli disappeared from the sputum; they returned, however, and the weight diminished also.

Not relieved.

CASE III.—*Pulmonary tuberculosis of four years' standing. Under treatment thirteen weeks.*

Summary.—Number of injections 35; amount used 227.8 mgms.; highest dose 12.2 mgms.; highest temperature 102.8°, after the 13th injection of 4.8 mgms. Made an apparent gain in general condition, and weighed seven pounds more at the end of treatment, but the bacilli did not disappear from the sputum.

Not relieved.

CASE IV.—*Pulmonary tuberculosis of five* (?) *years' standing, and tuberculous glands of the neck. Under treatment fifteen weeks.*

Summary.—Number of injections 36; amount used 264.5 mgms.; highest dose 14 mgms.; highest temperature 101.6°, after the 9th injection of 4 mgms. Bacilli absent from the sputum most of the time, and a gain of nearly ten pounds in weight. Lesions of the neck not improved.

Relieved. (Signs in the lung had not advanced in August.)

CASE V.—*Pulmonary tuberculosis of months' standing. Under treatment for five weeks.*

Summary.—Number of injections 19; amount used 93.4 mgms.; highest temperature 102°, after the 6th injection of 3.2 mgms. Bacilli were never found in the sputum. Gained in weight.

Not relieved. (In the summer the patient was drinking hard.)

CASE VI.—*Pulmonary tuberculosis of three years' standing. Under treatment for fourteen weeks.*

Summary.—Number of injections 38; amount used 347.6 mgms.; highest dose 10 mgms.; highest temperature 101.4°, after the 33d injection of 6 mgms.

Not relieved. (Marked advance in the signs in the lungs in August. See Chart III.)

CASE VII.—*Pulmonary tuberculosis of two months' standing. Under treatment for fourteen weeks.*

Summary.—Number of injections 35; amount used 287.6 mgms.; highest dose 10.8 mgms.; highest temperature 100.4°, after the 12th injection of 10 mgms. General condition good. Slight but constant gain in weight during treatment. Bacilli absent from the sputum most of the time.

Relieved.

CASE VIII.—*Pulmonary tuberculosis of eight months' standing. Under treatment for thirteen weeks.*

Summary.—Number of injections 32; amount used 301.8 mgms.; highest dose 14.4 mgms.; highest temperature 101.4°, after the 22d injection of 12 mgms.

Not relieved. (In July no advance in the signs in the lungs.)

CASE IX.—*Pulmonary tuberculosis of six months' standing. Under treatment for twelve weeks.*

Summary.—Number of injections 32; amount used 111.8 mgms.; highest dose 6 mgms.; highest temperature 101°, after the 3d injection of 3.2 mgms.

Relieved. (Gain in weight, and especially a great improvement in general condition.)

CASE X.—*Pulmonary tuberculosis of a year's standing. Under treatment for five weeks.* (*Disease of the "florid" type.*)

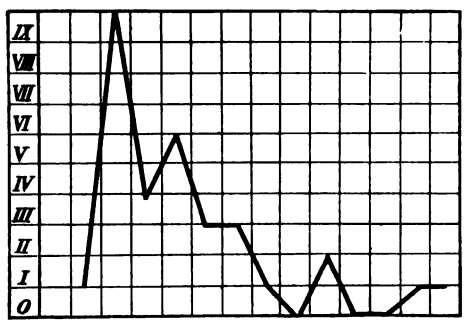
Summary.—Number of injections 8; amount used 14.2 mgms.; largest dose 2.4 mgms.; highest temperature 102.8°, after the 3d injection of 1.8 mgms.

Not relieved.

CASE XI.—*Pulmonary tuberculosis of four years' standing. Under treatment for ten weeks.*

Summary.—Number of injections 27; amount used 171.9 mgms.; highest dose 10 mgms.; highest temperature 101°, after the 4th injection of 7.2 mgms. Bacilli in the sputum diminished very much; the knee not improved.

CHART I.



Case XI.

Much relieved. (See Chart I.)

CASE XII.—*Pulmonary tuberculosis of three years' standing. Under treatment five weeks.*

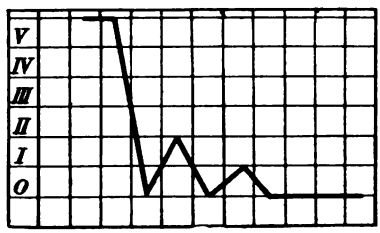
Summary.—Number of injections 18; amount used 62.4 mgms.; highest dose 4.8 mgms.; highest temperature 106°, the 2d day after the 15th injection of 4.8 mgms.

Relieved. (Bacilli disappeared very markedly from the sputum. See Chart II.)

Of these cases, most were of from six months' to five years' duration. The two in which the history extended for a shorter time than this,

were Case V., in which the bacilli were never found, and Case VII., in which there was a record of a cough for only two months. Case V. may possibly have been one of specific disease, and Case VII. is classified as improved, as will be shown below.

CHART II.



Case XII.

The general summary of the results, as seen in these cases, is as follows:

(1) *Not relieved*, seven, including Cases I., II., III., V. (in which the bacilli were never found), VI., VIII., and X. (Case II. was one with the complication of laryngeal and probably abdominal trouble.)

(2) *Relieved*, five, including Cases IV., VII., IX., XI. and XII. Case IV. (complicated with marked lesions of the skin in the cervical region) is classed as relieved, because of the marked diminution of the bacilli in the sputum, and the improvement in the general condition. The skin lesions made some improvement for a time, but then retrograded. (In August were more advanced, although the pulmonary signs were not so.) Case VII. is marked relieved for the reason that the patient showed a slight but constant gain in weight; the bacilli were absent from the sputum most of the time; the general condition was extremely good; and the patient asked to be allowed to go out in order to go to work.

Case IX. is classed as relieved, because of the gradual gain in weight during treatment, and the marked improvement in the general condition, as shown by the patient's ability to take severe exercise without fatigue or pain.

Case XI. (complicated with an affection of the knee), is classed as relieved for the reason that the bacilli showed a very marked and per-

manent diminution in the sputum, and the signs attracting attention to the chest had much diminished. The knee was not improved.

Case XII. (complicated with laryngeal affection) is classed as improved, for the reason that the bacilli have shown a marked and continuous diminution in the sputum, the laryngeal appearances have cleared up somewhat, and the general condition is improved, with a gain of six pounds in weight.

There were no cases in this class that could be called cured, and no deaths.

Of the cases grouped as "surgical," some certainly do not come under the head of tuberculosis by reason of any settled method of diagnosis that is at present at our command. They include (22):

SURGICAL CASES.

CASE XIII.—*Lupus of nose and mouth of six years' standing. Under treatment for fourteen weeks.*

Summary.—Number of injections 28; amount used 123.6 mgms; highest dose 8.4 mgms.; highest temperature 101.4°, after the 5th injection of 2 mgms.

Not relieved. (Lesions showed a very marked improvement for first six weeks of treatment; but then a retrogression began and active treatment in the way of local applications was employed.)

CASE XIV.—*Lupus of face and thigh of thirteen years' standing. Under treatment for fourteen weeks.*

Summary.—Number of injections 41; amount used 363.4 mgms.; highest dose 22.8 mgms.; highest temperature 104.8°, after the 5th dose of 2.2 mgms.

There was a gain in weight and a marked improvement in the condition of the affected area of the thigh; not so marked upon the face.

Relieved.

CASE XV.—*Tuberculous (?) metritis, of ten months' standing. Under treatment nine weeks.*

Summary.—Number of injections 23; amount used 106.8 mgms.; highest dose 10 mgms.; highest temperature 104°, after the 5th injection of 3 mgms.

Treatment omitted because of a severe attack of measles; up to that time the patient had shown a very decided improvement in general condition, with a gain of nearly ten pounds in weight, but with no especial alteration in the local condition.

Relieved.

CASE XVI.—*Enlarged glands of the neck of five months' standing. Under treatment four weeks.*

Summary.—Number of injections 11; amount used 48.9 mgms.; highest dose 7.5 mgms.; highest temperature 103°, after the 10th injection of 7.5 mgms. No effect upon the tumors was observed.

Not relieved.

CASE XVII.—*Disease of the knee of eighteen months' standing. Under treatment twelve weeks.*

Summary.—Number of injections 23; amount used 102.5 mgms.; highest dose 7.2 mgms.; highest temperature 103.4°, on the second day after the 13th injection of 5 mgms.

Not relieved. (General condition of the patient improved after the cessation of the treatment.)

CASE XVIII.—*Tuberculosis of glands of upper thoracic region, and pulmonary tuberculosis, of nearly two years' standing. Under treatment for six weeks.*

Summary.—Number of injections 10; amount used 27.7 mgms.; highest dose 4.8 mgms.; highest temperature 104.4°, after the 7th injection of 4 mgms.

Not relieved. (Died in about three weeks after leaving the hospital.)

CASE XIX.—*Empyema, with drainage-tube found in pleural cavity upon operation. Under treatment for thirteen weeks.*

Summary.—Number of injections 18; amount used 144.8 mgms.; highest dose 21.6 mgms.; highest temperature 102.6°, after the 5th injection of 3 mgms.

Not relieved.

CASE XX.—*Enlarged glands about cervical region and mediastinum, of two years' standing.* (*Pseudo-leucæmia.*) *Under treatment for three weeks.*

Summary.—Number of injections 7; amount used 27 mgms.; highest dose 7.2 mgms; highest temperature 101.7°, after the 4th injection of 4.8 mgms.

About a week after leaving the hospital the patient had high temperature, much increased swelling of the cervical glands, with pain, dyspnœa, loss of right radial pulse. In three days temperature sank, and the enlarged glands have almost completely disappeared. General condition much improved. This improvement in general condition and the condition of the cervical glands has persisted, with occasional attacks of elevation of temperature, until the present time. So that the patient, a physician, is inclined to the belief that there has been a change for the better; whether due to the treatment or not is an open question.

Relieved.

CASE XXI.—*Tuberculous disease of the toe of twelve years' standing. Under treatment for nine weeks.*

Summary.—Number of injections 21; amount used 127.6 mgms.; highest dose 12 mgms.; highest temperature 103.8°, after the 4th injection of 4.2 mgms.

Not relieved.

CASE XXII.—*Tuberculous disease of the knee, wrist, and inguinal glands. Under treatment for nine weeks.*

Summary.—Number of injections 30; amount used 203.5 mgms.; highest dose 16.8 mgms.; highest temperature 103.6°, after the 1st injection of 1.5 mgms.

Not relieved. (Leg was amputated about six weeks after the treatment was omitted.)

CASE XXIII.—*Tuberculous (?) disease of the cervical and sub-maxillary glands. Under treatment for nine weeks.*

Summary.—Number of injections 22; amount used 185.8 mgms.; highest dose 19.6 mgms.; highest temperature 104.2°, after the 3d injection of 1.2 mgms.

Relieved. (The cervical glands had cicatrized, there was no discharge, and the general condition had improved, with a gain of eight pounds in weight.)

CASE XXIV.—*Tuberculosis of skin of back of hand. Under treatment for ten weeks.*

Summary.—Number of injections 23; amount used 208.4 mgms.; highest temperature 100.8°, after the 6th injection of 7.2 mgms.

Not relieved.

CASE XXV.—*Tuberculosis of tongue (and of lung). Under treatment for seventeen weeks.*

Summary.—Number of injections 45; amount used 380.8 mgms.; highest dose 12 mgms.; highest temperature 101.4°, after the 1st injection of 0.8 mgms.

Not relieved.

CASE XXVI.—*Tuberculosis of the ankle of months' standing. Under treatment two weeks.*

Summary.—Number of injections 7; amount used 32 mgms.; highest dose 10 mgms. (Temperature chart lost and highest temperature not attainable.)

Relieved. (Wound healing very rapidly; general condition improved; and

CASE XXVII.—*Tuberculous (?) disease of hip. Under treatment for six weeks* (bacilli not found toward end of treatment).

Summary.—Number of injections 20; amount used 60.5 mgms.; highest dose 4.8 mgms.; highest temperature 105° (springing from 97°), after the 7th injection of 2.4 mgms.

Relieved. (General condition improved, and discharge from hip less.)

CASE XXVIII.—*Tuberculous disease of hip, cervical glands, and cornea. Under treatment for six weeks.*

Summary.—Number of injections 23; amount used 83 mgms; highest dose 6 mgms.; highest temperature 103°, after the 4th injection of 1.5 mgms.

Much relieved. (Eye well, cervical glands diminished, hip less sensitive, and discharge much less.)

CASE XXIX. — *Tuberculous* (?) *disease of the wrist, of months' standing. Under treatment for thirteen weeks.*

Summary.—Number of injections 7; amount used 20.4 mgms.; highest dose 6 mgms.; highest temperature 101.8°, after the 3d injection of 2 mgms.

Not relieved. (The attending surgeon considered the condition of the wrist on opening, March 27th, as evidence of improvement. Was doing extremely well when last heard from.)

CASE XXX.—*Tuberculous* (?) *disease of thumb and toe, of five months' standing. Under treatment for fourteen weeks.*

Summary.—Number of injections 28; amount used 125.4 mgms.; highest dose 7.8 mgms.; highest temperature 103.8°, after the 11th injection of 4.8 mgms.

Not relieved. (Thumb grew so much worse that it was amputated.)

CASE XXXI.—*Tuberculous* (?) *disease of elbow of five years' standing. Under treatment for eleven weeks.*

Summary.—Number of injections 22; amount used 93.4 mgms.; highest dose 8.4 mgms.; highest temperature 104.2°, after the 14th injection of 6.6 mgms.

Not relieved. (Excision of elbow performed during continuance of treatment.)

CASE XXXII.—*Pseudo-leucœmia of fourteen months' standing. Under treatment for seven weeks.*

Summary.—Number of injections 12; amount used 70.8 mgms.; highest temperature 103°, after the 7th injection of 5 mgms.

Died. (An attack of acute fibrinous pneumonia and pleurisy was the cause of death. There were no signs of any effect from the treatment.)

CASE XXXIII.—*Tuberculous* (?) *disease of the hip of one year's standing. Under treatment for nine weeks.*

Summary.—Number of injections 22; amount used 76.1 mgms.; highest dose 6 mgms.; highest temperature 105°, after the 16th injection of 4.8 mgms.

Not relieved. (General condition improved, but not because of treatment.)

CASE XXXIV.—*Tuberculous* (?) *disease of the hip of two years' standing. Under treatment for nine weeks.*

Summary.—Number of injections 23; amount used 111.4 mgms.; highest dose 8.4 mgms.; highest temperature 101.4°, after the 4th injection of 1.5 mgms.

Relieved. (General condition improved; night cries gone; discharge from the hip less.)

These cases should be classified as follows:

(1) Not relieved 12—including Cases XIII., XVI., XVII., XIX., XXI., XXII., XXIV., XXV., XXIX., XXX., XXXI., XXXIII.

Of these, Case XIII. (lupus of the face), showed a very great and rapid improvement, at least apparently, at first, and then stopped.

Case XIX. (empyema, with drainage-tube found in the pleural cavity) might readily be thrown out entirely. It cannot be taken as proving anything for or against the material, although after surgical interference the patient is very much better.

Case XXI. (suppuration of the toe, with slight pulmonary signs, but no bacilli) is reported better, as regards the pulmonary signs, by the attending physician.

Case XXIV. (lesion of the back of the hand) showed improvement at first, but was not better at the time last seen.

Case XXV. (tuberculosis of the tongue, with pulmonary lesions at the apex) showed a marked improvement at first; but this improvement was arrested, and the disease is now further advanced than at the beginning of the treatment.

Case XXIX. (disease of the wrist, with sinus) presented a peculiar appearance upon opening the wrist, inasmuch as there was a complete absence of anything that would account for the keeping open of the sinus, which healed kindly after the removal of the thickened lining membrane.

(2) Relieved 6, including Cases XIV., XV., XXIII., XXVI., XXVII., XXXIV.

Case XIV. (lupus of the face and thigh) is classed as relieved, because of the marked diminution of the infiltration and thickening of the thigh; of the equally marked and similar change in the condition of the face, and the improvement in the general condition of the patient. The relief, however, was but temporary.

Case XV. (tumor in Douglas's pouch—no real evidence of tuberculosis) showed a very great and marked improvement in general condition, up to the time of the attack of measles. There was a constant and gradual increase in weight of ten pounds, a diminution of the local distressing symptoms; and this, following the contrary condition of affairs, and beginning with the injections.

Case XXIII. (enlarged and suppurating cervical glands) showed sudden enlargement of one gland, with discharge following the treatment; followed by a cessation of any reaction, local or general; by the closing of the sinus; the diminution in size of the gland, and cessation of its activity; together with a marked increase in weight.

Case XXVI. (disease of the ankle—bacilli found in the discharge) improved afterward enough to have motion in the joint; no bacilli were found afterward in the discharge from the ankle; and there was a change for the better in the general condition.

Case XXVII. (hip disease) showed a marked improvement in the general condition; a diminution in the discharge from the hip, and a diminution in the subjective symptoms.

Case XXXIV. (hip disease) general condition improved; discharge from the hip less; subjective symptoms less.

(3) Much relieved 2—including Cases XX. and XXVIII.

Case XX. (pseudo-leucæmia), after leaving the hospital, suffered from a sharp febrile attack, accompanied with a great enlargement of the glands (situated principally in the cervical region), lasting for three or four days; followed by a rapid diminution in size of the glands and a marked improvement in the general condition, that has held up to within a week; more than six months after the cessation of treatment. The case is an exceedingly puzzling one. The patient himself certainly feels that a change for the better has taken place in his condition. The enlarged glands were, at the time of last inspection, remarkably diminished in size, and this has continued.

CASE XXVIII. (hip disease, ulceration of the cornea, enlarged cervical glands) showed a great gain in general condition; the ulceration of the cornea is arrested; the cervical glands are normal in size, and the discharge from the hip is much less.

(4) Died, 2—including Cases XVIII. and XXXII.

CASE XVIII. was desperate from the start. The patient had been running down as rapidly as possible for some time before entrance; had been operated upon four or five times for the removal of the affected glands; had pulmonary lesions in addition to amyloid kidneys, spleen, and, probably, liver. Died of exhaustion, about two weeks after removal from the hospital, and four weeks after the last injection.

CASE XXXII. (pseudo-leucæmia) is one of the most interesting that have come under observation, more especially in view of the recent investigations[1] that have been published, tending to show a relationship between certain forms of this disease and tuberculosis. There was a marked temperature reaction during the treatment. Bacilli were found in the sputum once, although they were in such small numbers that this might have been a contamination; and yet at the autopsy there was no sign of tuberculosis in the gross appearance, nor have any certain microscopic signs been found.

The death in this case was distinctly due to an intercurrent attack of pleurisy and pneumonia, and not to the injections.

In this series, as in the former one, there are no cures to report.

While it is perfectly true that an ordinary microscopic examination of the sputum for bacilli must give a very imperfect idea of the numbers that may be present, and that in order to secure an exact approximation to these numbers one must have recourse to some method of procedure like the very clever one of Nuttall, nevertheless my experience of the application of a series to clinical work leads me to feel that even for the ordinary expert examination there is more or less of accord in the numbers found and the condition of the patient. What I mean is best indicated by a reference to the charts that I have to show, that are made up from the examinations of the sputum in certain of the cases that I have had under treatment.

The use of Gaffky's tables for the expression of quantities of bacilli found in sputum at successive examinations makes it possible to work out certain curves that are of interest to examine.

Taking the absence of bacilli as representing 0, and going on with

[1] Brentano and Tangl, Deut. med. Woch., No. 17, 1891.

his enumeration, we can build up a series of transverse lines running to ten. The lateral space is devoted to the dates of the examinations, each date being separated by a perpendicular line. Then dots placed high or low, as the case may be, represent the number of bacilli, and when connected give a graphic representation of their variations in the sputum. Such curves as this have been worked out for me from the material furnished by the cases by Mr. A. D. Hodges, a second-year student in the medical school.

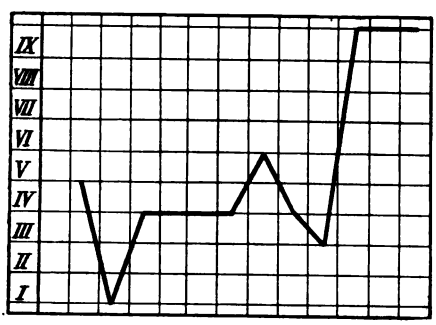
They are of special interest, for the reason that the variations correspond curiously enough with the periods of change in condition as shown by the records.

A chart from the sputum examinations of Case I. (pulmonary tuberculosis) shows a constant persistence of the bacilli and their presence in fairly large numbers. (This patient showed no appearance of improvement at any time.)

A chart from Case II. (pulmonary, laryngeal, and probably abdominal tuberculosis) shows first a high curve, a marked diminution that apparently corresponds with the temporary improvement that was manifest at one time, and then again a sharp rise.

A chart from Case III. (pulmonary) shows a general rise in the curve.

CHART III.



Case VI.

A chart from Case IV. (pulmonary and tuberculous scrofulo-derma of the neck) shows a constant low average in the sputum, the bacilli being absent most of the time. (The pulmonary signs not increased in August in this case.)

A chart from Case VI. (pulmonary) shows a constant and marked

rise from about the middle of the treatment, the last examinations giving them in enormous numbers. (See Chart III.) (Patient's physical condition has grown rapidly worse up to the present time.)

A chart from Case VIII. (pulmonary) shows two periods of rise and decline, the last leaving the curve higher, however, than at the beginning of the examinations.

A chart from Case IX. (pulmonary) shows also a period of increase after the treatment was begun; then a fall, and a second rise, that up to the time of the last examination had not reached as far as did the first one.

A chart (Chart I.) from Case XI. (pulmonary and knee) shows a very remarkable and persistent fall after the first of the treatment.

A chart (Chart II.) from Case XII. (pulmonary and laryngeal) also shows a very remarkable and persistent fall after the first of the treatment.

A chart from the sputum of Case XXV. (tuberculosis of tongue and lung) shows a constant climb, highest at the last examination and lowest at the times of the apparent improvement of the patient.

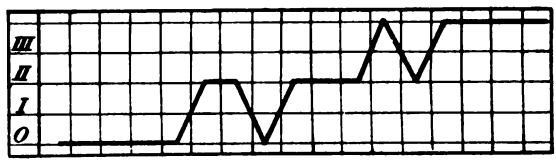
A chart from the secretion from the tongue of Case XXV. shows always a low average, but seemingly lowest at the times of apparent improvement in the lesion of the tongue.

The charts from Cases XI. and XII. are so remarkable that, although by themselves they show nothing, it seemed to be a matter of importance to find out whether anything similar would occur in the ordinary course of the disease as it advances, or exists under ordinary treatment. Fortunately, the means for this comparison were easily at hand in two ways. The first was from some work of my own, embodied in a paper read before the Massachusetts Medical Society in June, 1883; for the purposes of which I had made a similar series of examinations and charts. These are five in number. They represent the results of examinations extending over about three months at the same season of the year as the first series, are classified in a similar manner, and show exactly the opposite to what is seen in the new charts of Cases XI. and XII.; that is to say, there is a very evident rise of the curve, as the time of the examinations extend, instead of a fall. (Two are given, see Charts IV. and V.)

The second means for comparison is with work not done under my direction or by me; namely, in the results of the sputum examina-

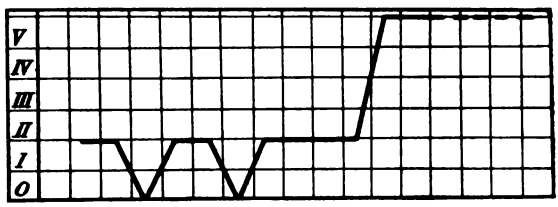
tion, given by Gaffky in the same place that is cited above. A series of examinations is there recorded of the daily number of the bacilli in the sputum, and when these are plotted out the curves show the

CHART IV.



(Ernst, No. 3.)

CHART V.



(Ernst, No. 5.)

same point as do those made by myself—a constant and steady rise as the disease progressed (illustrated by Chart VI.), or at least a holding of the same level, with never but once a drop at all like that shown in the charts of Cases XI. and XII.—this one drop being in a case that died shortly after the examinations were begun, but in which there had been a constant and steady improvement in the condition of the patient, death occurring from peritonitis after swallowing a large number of prune-stones.

The conclusions that may be drawn from these charts are, of course, not final; but the facts themselves are certainly of interest, and possibly of importance.

In many of the cases at least a part of the improvement noted has been due to the more favorable surroundings of hospital life and care; but to set aside any doubt I wish to say that this influence has been fully considered and given due credit in making up the results. In some of those marked as relieved it has undoubtedly played a part;

but, with all this excluded, there are some effects that have been seen that are inexplicable to my mind by this beneficial influence alone.

My experience with tuberculin has apparently corresponded with that of most others. There is a marked and rapid improvement in

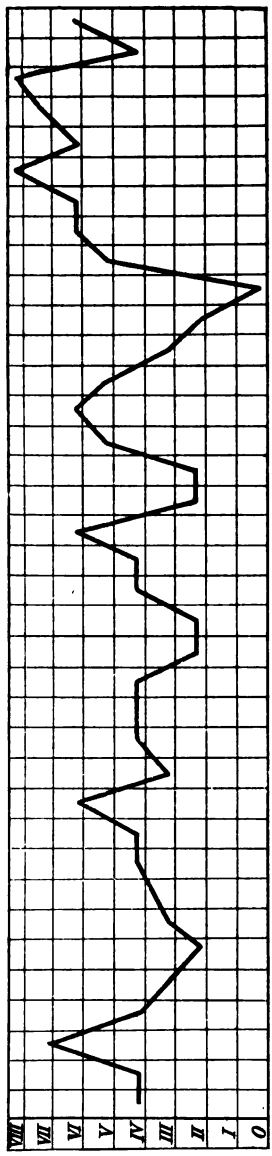


CHART VI.

(Gaffky—"Patient A.")

certain cases, more especially those of external tuberculosis (including lupus), which goes on for a certain time and then stops, and the effect of the material is lost. The lesions even begin to retrograde. Seen at a certain time after the treatment has been going on, the results for the future are very apt to be gauged by what has been accomplished in the first of the treatment; and this is precisely what happened in my observations in Berlin. I saw there the same—only more marked—improvement in cases of lupus, pulmonary tuberculosis, and surgical disease that has occasionally occurred here; but neither there nor here has the early promise been kept up.

The results obtained by the clinical use of tuberculin having fallen so lamentably far short of what was hoped for, it has been the desire of those not too much discouraged with the whole subject to care any more about it, to attempt to find some reason for this failure and to see what alterations could be made in the methods of preparation or of administration to bring about more favorable results.

In the first place, and from almost the beginning—at least from the time of Virchow's first publication of the apparances in his autopsies upon persons dead after the use of "tuberculin"—the dangers that might arise have been very vividly present to the minds of all those who have been using it. These dangers—while I have fortunately had no personal experience of them—are unquestionably real, and one must have the possibility of a metastatic infection in mind in the course of the treament of any given case. That the dangers of this are, however, diminished by moderation in the dose is, I think, true, and it is not yet time to say that possibility of benefit from the slower application of the material is out of the question.

However, from the very fact that the material was well known to be a mixture, and so little was understood of its composition, the necessity for a complete examination of what it actually is was easily manifest. How little even Koch himself knew of this composition at the period of his first announcements is shown by the work of Hunter and Cheyne, so recently published. Koch's statement that the active curative principle of "tuberculin" is thrown down by absolute alcohol is shown to be incorrect, if these latter experimenters are not in the wrong, and the heavy white precipitate seen so abundantly upon the addition of alcohol to "tuberculin" is by them shown to contain the

portion of the elements that produce the febrile and other disturbances, and not to be concerned with the beneficial effects that are sought for.

Dr. Hunter's work seems to me to be of such importance, in connection with the clinical side of it, as being worked out by Mr. Cheyne, that I have quoted from it largely. His article is in the *British Medical Journal* for July 25th, and contains an account of his efforts to study the nature of "tuberculin." The chief substances he found in it were: 1, albumoses; 2, alkaloidal substances (two of which can be obtained in the form of the platinum compounds of their hydrochlorate salts); 3, extractives (small in quantity and of unrecognized nature); 4, mucin; 5, inorganic salts; 6, glycerin and coloring matter. He did not find serum-albumin, globulin, or peptones.

The materials mentioned above being found, various modifications of the original tuberculin were made and tried. Of these there were especially three, prepared as follows:

Modification A, which consisted of the total precipitate thrown down from tuberculin by absolute alcohol, and made by adding 1 c.c. tuberculin to 10 c.c. absolute alcohol. (Solution A_2, which showed the least loss of the albumoses and the greatest removal of the other substances, was made by adding 1 c.c. tuberculin to 7 c.c. absolute alcohol and 2 c.c. water. It was almost colorless, and had lost the power of producing even the slight degree of fever usually the result of the use of *A*.)

Modification C was the counterpart of *A*, and contained all of the constituents of tuberculin not present in *A*. Made by evaporating the filtrate over a water-bath at not over 40 degrees, and taking up the residue with ½ per cent. carbolic acid solution.

The proportion of salts contained in *C* or of albumoses in *A* varied somewhat with the rapidity of filtering, for the reason that some of the salts were only slowly soluble in alcohol.

The contrast in the action of these two, *A* and *C*, was very interesting. Both seemed to show a slight remedial action, causing absorption and disappearance of tuberculous tissue; but with *A* there was decidedly severe local reaction with little fever, while with *C* there was marked fever and little local reaction. (Solution A_2, with fewer salts, produced less fever, so that it seemed as if it was the salts that produced the febrile reaction.) This result led to the production of *Modification B*, which was formed by precipitating all of the albu-

moses present by ammonium sulphate so far as possible without heat or nitric acid. The precipitate, taken up in distilled water, placed in a sausage-skin dialyzer and dialyzed for twenty-four hours, first in running water two hours and then in distilled water twenty-two hours, was found to possess in an eminent degree the power of inducing local reaction followed by a healing change around the tuberculous lesions, unaccompanied by any constitutional disturbance whatever.

A combination of *C* and *B* was made under the name of *Modification CB*, and was found to be capable of inducing very distinct local improvement, unattended with fever, and, still more markedly, accompanied by scarcely any noticeable inflammatory reaction. The exact details of the preparation of this modification are as follows: 2 c.c. tuberculin dropped into 20 c.c. absolute alcohol. The heavy precipitate filtered off in a quarter of an hour; filtrate evaporated over a water-bath at a temperature not exceeding 40° C., and just long enough to drive off all the alcohol; the residue taken up with 12 c.c. aqua destillata, placed in a sausage-skin dialyzer, and dialyzed for two hours in a running stream of water. At the end of this time its previously yellow color is much diminished. The quantity is made up to 20 c.c., including 2 c.c. pure glycerin for preservative purposes; a few crystals of thymol are also added. (Title was "*CB* 10 per cent.")

It is a pleasure to quote the work here related, for it is free from the objectionable feature that hangs about the original announcements —the absence of details in regard to the experiments by which such momentous results were claimed to be reached. If anything is ever to come from the investigations from the newer lines of research, it must be by the full description of how each step has been made, and with the shock that our credulity has received in the last year it is too much to ask for that credence shall be given in the future to any such extent as has obtained in this instance.

Cheyne, in common with others, failed to secure immunity with "tuberculin" in guinea-pigs, and it has interested me to test, so far as I have been able, another step in the question—the healing power of the material when directed against the intentionally produced cutaneous tuberculosis spoken of by Koch. To this end I have made a short series of experiments that are here given:

It will be remembered that Koch, in speaking of how he made his

discovery of the action of "tuberculin," mentions a circumscribed, localized tuberculosis that follows the cutaneous inoculation of a pure culture of the bacilli of tuberculosis in guinea-pigs, and states further that such a tuberculous nodule may be healed by the use, by injection, of sterilized cultures of the bacilli.

Following out this indication as well as possible, but using tuberculin instead of the sterilized cultures—for, of course, the results should be more marked with the former—I have endeavored to obtain similar results to those arrived at by Koch. A number of guinea-pigs kept under observation for a sufficient length of time to make it as certain as possible that they were in good health, were inoculated *cutaneously* with pure cultures of the bacilli of tuberculosis.

In every case the peculiar nodule spoken of as the sequel of such a cutaneous inoculation made its appearance, but in no case thus far observed has there been any evidence of a healing action as a result of the injections of tuberculin. One of the animals has shown a very marked diminution in the size of the nodule, but so also has one of the control animals which has not been treated with the material at all.

In fact, so far as my observations go, it is exceedingly difficult to make guinea-pigs react to tuberculin. I have injected three animals with one, two, and three c.c. of the original material without being able to perceive any effect whatever; a result, of course, in accordance with what was said would be the case if the animals were healthy, as these were supposed to be.

The experiments are not yet completed, and I have therefore refrained from giving the full details.

My experience with tuberculin would lead me to take the following position in regard to it:

1. It has no diagnostic value that is at all applicable at present to clinical use.

2. I have been entirely unable to demonstrate anything more than a possible temporary beneficial result, and this only in certain cases, from its use in human beings in any form of tuberculous disease.

3. I have had no personal experience with its ill effects, but there can be no doubt that these occur.

4. Its advantages, so far as I have seen them, would not induce me to use it again in practice.

There are, however, certain other points that should be well understood before this material, or rather its source, should be given up for investigation. Some of these seem to me to be indicated as follows:

1. Tuberculin itself is a very complex material, and its constituents must be separated and well understood before it can be definitely asserted that it does not contain something of value in compelling the healing process in tuberculous lesions; this is well shown by the results obtained by Hunter and Cheyne, and already referred to.

2. The same thing is indicated even more strongly by the effects that seem to have shown themselves in the clinical experiments conducted with it; for while there has not been much actual healing to report, nevertheless such effects have been demonstrated, that it is within the bounds of possibility to believe that by different methods of preparation a material may be obtained from pure cultures of the bacilli that may give more satisfactory results.

KOCH'S TREATMENT OF TUBERCULOSIS.

By WILLIAM OSLER, M.D.,
PROFESSOR OF MEDICINE IN JOHNS HOPKINS UNIVERSITY.

In the medical wards of the Johns Hopkins Hospital inoculations were practised on twenty-eight patients. Twenty-two of these were cases of pulmonary tuberculosis, three were cases of pleurisy suspected to be tuberculous, two were for diagnostic purposes with negative results, and one case, which was thought to be tuberculous adenitis, proved to be cancerous. In giving the injections we began with small doses, and, as a rule, gradually increased if the patient had no reactions, in some instances going as high as 35 or 40 milligrammes. We selected the cases which were, so far as physical examination could guide us, either in the early stage, or instances in which the disease was quiescent. The injections were not practised on any advanced case.

The practical results may be stated in a very few words. No case was cured. Five cases were decidedly benefited; the results being evident not so much in change in the physical signs as in improvement in the general condition and in weight; thus the cases which improved gained from nine to fourteen pounds. In not one did the bacilli entirely disappear from the expectoration. In all, the cough was reduced in frequency. I have not been able to get the details of three of these patients; two of them I have seen within the past week. In one the improvement continues. Thus the second case in which we used it weighed on admission 114 pounds, and weighed on discharge 117½ pounds, and on the thirteenth of this month weighed 126 pounds. In this case, too, there is an improvement in the physical signs, the râles having diminished in a marked manner. Another of the cases which had improved very much has lost ground through the summer, and on examination a few days ago the disease had evidently made progress.

The five cases in which improvement was most marked were cases in which the disease was not very recent, having lasted from seven months to more than two years; but in all of them the trouble was more or less localized. Of the remaining seventeen cases, nine left the hospital distinctly rendered worse by the treatment. Of these one died shortly after, and another a few weeks ago. Of the other seven I have not heard. In four the condition was not materially changed, and in four there was slight improvement noted, particularly in the gain in weight. No deaths occurred while the patients were directly under treatment. In one case, not counted in this list, a patient had a single injection, and in two days developed signs of extensive pneumonia of the right base, which we were at first inclined to think might be a tuberculin effect, but the persistent high fever and the progressive and rapid development of the consolidation rather favored the view that it was an acute pneumonia. The autopsy made by Dr. Welch fully confirmed this.

The bad results of the treatment were evident in the increase in the consolidation, breaking down of the lung tissue, great increase in the fever, progressive weakness, and loss of weight. This was specially marked in several cases in which the disease was in an early stage. Of the three pleurisy cases, one gained 13½ pounds, a second 5½ pounds, and a third 10 pounds. These were instances of suspected tuberculous pleurisy, and there were reactions after the injections, but tubercle bacilli were not found in the expectoration.

On the whole we were, of course, disappointed with the results. We cannot reproach ourselves with a lack of care in the selection of the cases, as we exercised reasonable caution in choosing patients in a tolerably favorable condition, and in as early a stage as possible. The increase of the dose, which was carried out in many, but not all, of the cases, may have been a mistake, but in this matter we followed, we believed, the best directions.

THE FREQUENCY OF THE LOCALIZATION OF PHTHISIS PULMONALIS IN THE UPPER LOBES.

By J. WEST ROOSEVELT, M.D.,
PHYSICIAN TO THE ROOSEVELT AND BELLEVUE HOSPITALS, NEW YORK.

THERE is no need at this time and in presence of this audience to state that, without the presence of Koch's bacillus, there is no tuberculosis. Possibly the statement that without tuberculosis there is no phthisis might not even yet be so generally admitted, though it is probably true.

In this paper the writer has confined his attention to the following points:

1. Consumption, in an enormous majority of cases, begins in the upper lobes of the lungs, near the extreme apices.

2. Consumption, whether called "catarrhal" or "tubercular phthisis," or "caseous pneumonia," or by any other name, has, as part of its lesion, newly formed tissue containing the *Bacillus tuberculosis* of Koch. This new tissue has the anatomical structure which we call "tubercle." It is, as is well known, composed of a basement substance containing lymphoid and epithelioid cells, and not infrequently also giant cells. Tubercle tissue is comparatively bloodless, and for this reason soon breaks down. It is peculiarly prone to what is called "cheesy degeneration."

It is unimportant for the present discussion whether the bacillus is regarded as a cause, an accompaniment, or a result of the disease process.[1]

[1] If the bacillus only can obtain a suitable soil in the upper lobes because of pre-existing lesion, or because there is some congenital or acquired vulnerability of these regions, which does not occur, as a rule, in the lower, proof of one or the other of these possibilities would modify or utterly refute the most prominent (though not the most important) statements made in this paper. The theory of embolic origin of pulmonary tubercles and the physical laws stated to explain the reason for the frequent selection

The bacillus is found in the cases under discussion. The lesion in a vast majority of them begins in the apices. The question before us is simply this: *Why does the bacillus lodge in the apices of the lungs in human beings in a very great majority of cases before it invades other portions?*

Why it lodges more often in the lungs than elsewhere is quite clear. If it is inhaled, it is inhaled into these organs. If it is absorbed through mucous membrane or skin, the contents of the absorbing lymphatics and veins alike must pass through the lungs before entering the systemic arteries; and the pulmonary capillaries are a filter through which masses of bacilli or anything else only a little larger than a white blood-cell cannot pass.

Single bacilli or small groups, of course, can and doubtless do freely circulate with the blood-cells through these vessels; but a larger mass, containing bacilli and perhaps a number of leucocytes or some cheesy matter, must be arrested by them. Cheesy masses containing bacilli originate more often, in the human body, in situations where, if they enter at all, they must enter the body through lymphatics or venous radicles. For this reason they must more often be arrested in the lungs than elsewhere. Unless tubercle bacilli are spontaneously generated within the lungs, they must enter them through the air-tubes, bloodvessels or lymphatics.

The infectious material is thought by many to be inhaled. But the explanations advanced of why it is so frequently inhaled into the upper lobes are most contradictory. Scattered through the literature we have many remarks about the so-called phthisical habit, by which is meant a slender, rather tall figure, with poor muscular development; a long, slender neck; a small amount of superficial fat; and a flat, long, thin thorax, which thorax is said to be for some reason deficient in the movement of the upper ribs. This type, like every other conceivable type, of human being does undoubtedly sometimes develop phthisis. In many papers the cause of the disease is said to be a

by tuberculous matter of the upper lobes, necessarily occupies a larger space and a more prominent position than the (practically more important) deduction, based upon experimental evidences, that pulmonary consumption is probably produced in many cases by bacilli which enter the naso-pharynx, trachea, œsophagus, mouth, and gastro-intestinal tract, or skin. The point of greatest importance insisted upon is that the bacteria cannot be directly inhaled and lodged by the air-currents in the pulmonary vesicles.

"paralytic thorax" with deficient motion of the upper part of it. Such a thorax is the thorax of a person who already has phthisis in the upper lobes. It is a result, not a cause, of the disease.

All of the more generally accepted theories which explain the frequent selection of the upper lobes by infection through the air-passages assume some difference between the movements of the upper and lower parts of the thorax, and, as a result thereof, a like difference in movement of the upper and lower lobes of the lungs. So far they agree, but the exact results of this supposed difference are explained by various writers in several ways. All agree that the upper portions of the chest move, absolutely, less than the lower, and hence assume that the same thing is true of the movements of the upper and lower lobes. The idea that the *absolute* motion of any part of the chest or lungs has nothing to do with the question, does not seem to have been appreciated by the majority of these theorists. Granting that any part of the chest moves less than any other (and even supposing, *argumenti gratia*, that each part of the lung follows each part of the chest wall, which I deny), we have to consider relative and not absolute motion, for the surface of a larger bulk of lung must be moved a greater distance than the surface of a smaller, in order to produce the same amount of expansion or contraction in the vesicles of both. How the supposed difference in the motion determines the frequent selection, by the virus, of the upper lobes rather than the lower is a matter of controversy. Some writers say that the deficiency in motion of the upper parts of the chest causes, in the upper lobes, feeble respiratory power and what they call "insufficient ventilation." Others, perceiving that diminished *respiratory* power implies diminished *inspiratory* power, and therefore does not account for the facts, state, without any kind of proof, that the deficiency of expiratory power must result in rendering the apices less able than the rest of the lungs to expel infectious material. In a paper published in May,[1] 1889, the writer said that the alleged difference could not be shown to exist.

Some authors think that the lower lobes, because of their greater supposed motion, empty a part of their contents, during expiration, into the upper. This is so evidently preposterous, when we speak of

[1] "The Movements of the Thorax and Lungs considered in their Relation to Certain Pulmonary Diseases," Medical Record, May 25, 1889.

ordinary breathing, that still others have modified it and allege that only during cough does this peculiar phenomenon occur. Among the latter is Meltzer,[1] whose ideas carry a great weight, for he is, so far as I know, the only author who has approached the problem in a genuinely scientific way. I must disagree with an important part of his explanation, however.[2]

Most writers upon the subject seem to have very vague ideas of the physical factors involved. Let us take the statement of Rindfleisch in Von Ziemssen's *Cyclopædia*, vol. v., pages 654 *et seq.*, where he says that the weight of the arms hanging upon the upper part of the chest must restrict its movements. He adds that the secretions in the upper lobes are thickened because, as Virchow has remarked, the thickness of such secretions in the bronchi is "inversely as the blood supply." Subsequently, on page 656, Rindfleisch states that an insufficient quantity of blood in the lungs will cause the vessels of the lower lobes to be filled more than those of the upper. Under what conditions this "insufficient quantity of blood" exists, unless it is in cases of disease of the right side of the heart; why, granting its existence, it should cause "the vessels of the lower lobe to be filled more than those of the upper;" or what possible effect the chest movements can have in producing the alleged phenomenon, are questions passed over by this author in dignified silence.

This statement by Rindfleisch is mentioned merely to show how confused a most excellent microscopist may become when dealing with a physical problem. He evidently has disregarded not only the actual

[1] "Ueber die Localisation der Tuberkulose in der Lungenspitze und über den Mechanismus des Hineingelangens von corpusculären Elementen in die Lungenalveolen." Sonderabdruck aus den Verhandlungen des X. internationalen medicinischen Congresses.

[2] He makes this statement, which seems to me incorrect:

"Beim Husten . . . erfolgt zuerst eine tiefe Inspiration, darauf ein Verschluss der Glottis, eine Erschlaffung der Inspiration und eine energische Contraction der Expiratoren. Am Ende der tiefen Inspiration ist der Druck in allen Theilen der Lunge gleich dem Atmosphärendrucke, in allen Theilen *mit Ausnahme dergenigen Alveolengruppe, welche durch einen in den Alveolargangen adhärenden Embolus von der Luft abgesperrt ist.*" [The italics are mine.] "Every alveolus, whether plugged or not by any substance in the bronchiole through which it communicates with the air, is, under all circumstances, subjected to a pressure, after deep inspiration, which precisely equals that of the external air. If its afferent bronchiole is plugged, it may not expand so much as the surrounding alveoli, but the pressure exerted by the air within it is always the same."

anatomical relation of the chest and its surroundings, but also the resultant of the forces produced by muscles and bones. Anyone who takes the trouble to look at the shape of the clavicles and their attachments to the sternum and scapulæ, and also at the attachments of the trapezii and other muscles, will see that the weight of the arms is supported by the vertebral column and the cranium, and that the position of the clavicles in relation to the sternum and scapulæ is such that the upper part of the thorax sustains hardly any part of it.

In an effort to explain the vulnerability of the upper lobe, Rhuele (Von Ziemssen's *Cyclopædia*, American edition, vol. v. p. 487) says: "The apices project from three to four cm. above the clavicles, and this projecting portion, being situated *outside the chest, is subjected to the pressure of external air.*" (The italics are mine.) Now, why these portions should be said to be "outside the chest," if by "chest" is meant the thoracic cavity, is incomprehensible. Certainly they are no more "subjected to the pressure of the external air" than if they were situated close to the diaphragm. The lungs are always and at every part under a condition of what is called negative pressure produced by the chest walls. It makes no difference whether the upper or lower part "project" three cm. more or less. In reality, what this writer calls incorrectly "projecting parts" are in no sense whatever "subjected to the pressure of the external air;" if they were, they would not "project," for this pressure would permit them to be withdrawn by their own elasticity until it ceased to be exerted. This mistake calls to mind the numerous errors which have been made in calculating the amount of muscular force expended during inspiration. It has frequently been assumed that, since the inspiratory movement is purely muscular, the muscles have, unassisted, to overcome more or less of the pressure of the air upon the outside of the chest, as well as the elastic recoil of the lungs, so that many of these calculations are utterly valueless. In point of fact, the elastic recoil and the external air pressure are nearly balanced by the elasticity of the ribs and costal cartilages. This fact makes it clear that the muscles during inspiration receive much aid from the same elasticity.

One observer remarks that bulging of the upper part of the chest was observed during cough in a patient whose upper ribs were absent, and thinks that this is a proof that in that part of the chest there is during cough an increased air pressure relatively to the other parts

when the ribs are present. A moment's thought will show that the bulging took place simply and solely because the ribs were absent. Had they been present, the conditions would have been utterly different.

I have, in a former paper,[1] expressed the opinion that it is probable that the chest movements have nothing to do with the expansion of the part of the lung which happens to lie immediately beneath any one part of the chest wall. Perhaps this statement is a little too sweeping, but it is safe to say that they have very little to do with it. If there were no lungs in the chest—if the thorax was simply a cavity with an opening into it connecting with the external air—it is evident that expansion or contraction resulting from the movement of any part of the walls would practically affect equally all the contained air. The introduction into the cavity of an elastic organ like the lung, which communicates with the air, while the cavity itself does not, really alters the physical conditions very little. The movements of the organ, expanded as it is by the air, can hardly differ from those of the air itself in a cavity containing one lung. It is very unlikely that any part of the lung should be developed so that its bulk would be greater than could be properly expanded and contracted by the respiratory movements. Even if there really were some difference in the relative expansion and contraction of the upper and lower parts of the lungs, it is hard to imagine that as a result of these differences tubercle bacilli should be lodged so frequently in the apices, while the pneumococcus, in a majority of cases, is drawn into the lower lobes. Moreover, I must remind you of the well-known difference in the types of respiration which are characteristic of the two sexes. My reason for so doing is simply to accentuate (what I have several times stated in other papers) that this difference is a most serious objection to any theory which explains the selection in a majority of cases (in both sexes) either of the upper or lower lobes by any inhaled infective substance. In the female the expansion of the upper part of the chest is relatively much greater than in the male, when compared to the expansion of the abdomen. Among civilized women, at least, thoracic breathing is the rule, while among civilized men abdominal breathing is usual. If, as is so often assumed, the upper lobes are so

[1] Medical Record, May 25, 1889.

frequently infected by inhaled tubercle bacilli, which are lodged in them by some peculiarity in the movements of the upper parts of the chest, then surely it must be a remarkable peculiarity, for it seems unaffected by the two entirely different types of breathing which obtain in men and in women. In the one case a *relatively excessive movement* of the upper chest must produce this result; in the other a *relatively insufficient* movement must do the same.

It is very hard to believe that the bacilli can possibly be carried directly by the air through the ultimate bronchi into the air-vesicles. It is even harder to believe that in many cases the earliest tubercles should be found in the pulmonary pleura; yet a large number of the adhesions so frequently existing between the two layers of the pleura are the result of tubercular inflammation. The larger bronchi usually escape tubercular infection until long after the walls of the air-vesicles are diseased. If the bacilli are inspired, why do they first select the termination of the air-passages and avoid the walls of the larger tubes? If they are dry, they must behave—being governed by the same laws—precisely in the same way as any inspired, finely divided dust. If suspended in secretions, they, together with the secretions, must behave in the same way as all liquids do in the air-tubes. What is probably the behavior of dust or liquids in these tubes?

In regard to dust there is no proof, so far as I know, that any solid particles are ever drawn in by the air-currents even as far as the smallest bronchi. A number of experiments upon lungs removed from the body and suitably prepared confirm the results of other observers, that it is impossible to blow fine powders into the lobules. In no case have I been able to force beyond the bronchi powder of a size sufficiently large to be visible to the naked eye. In cases of pneumonoconiosis the dust is, so far as I can learn, distributed in somewhat the same way as tubercle is.

Respecting the behavior of fluids in the air-tubes, I have no experimental evidence to offer. It is worthy of remark, however, that—except in œdema of the lungs, where the serum probably directly enters them; in broncho-pneumonia, and in resolving lobar pneumonia, where, without doubt, the products of inflammation and resolution exude into them—it is very rare to find fluid in the air-vesicles. Considerable hæmoptysis may occur, yet no blood is found in the lobules. Profuse bronchial secretion either does not find its

way into them, or it must be absorbed with marvellous rapidity by their walls.

The tubercular lesion is primarily deep-seated (*i. e.*, situated far from the larger air-tubes). Rindfleisch states that it begins just where the ultimate bronchiole abruptly terminates in the lobule. While I do not admit the accuracy of his diagram of the lobule, it seems to me that the position of the commencing tubercle indicated by him is correct. The younger tubercles, so far as my observation goes, are usually found near the entrance of the bronchiole into the lobule. *This is precisely where the pulmonary artery, which accompanies the bronchiole, abruptly divides into capillaries. The terminal branch of the artery is quite large; the capillary network, although abundant, is composed of vessels of small calibre. It is here, where the younger tubercles are found, that one would expect a small embolus to be arrested.*

Nothing else than the tubercle bacillus seems to be inhaled in the manner in which this bacillus is stated to be inhaled. It is not without importance to note that the alveoli of healthy lungs are usually found to contain no bacteria at autopsies made soon after death. It is, therefore, probable that during life these germs rarely enter them, if, indeed, they ever do. Seemingly, dust cannot be driven into them under positive pressure. Of course, there is a great difference in the physical conditions which obtain in lungs inflated by positive pressure and lungs inflated, as they are during life, by negative pressure. Theoretically at least, dust entering the lungs under positive pressure must be carried further in than under negative, for the inspiratory current resulting from positive pressure is, in the smallest bronchi, more forcible, while the same current produced, as it is under normal conditions, under negative pressure, is less forcible than the expiratory.

It is improbable that the bacilli are ever drawn into the vesicles anywhere in the lung with the inspired air, and inconceivable that the direct action of the air-currents should determine in such a majority of cases the primary infection of the upper lobes.

Possibly the infectious substance is lodged in the upper lobes directly by lymph. We do not positively know the direction of the lymph-current in the lungs, but it is extremely probable (indeed we may say almost certain) that it is from the pleural surface toward the

root. There is so little doubt of the truth of this that direct infection of the lungs by a current flowing from the root toward the pleura is not worthy of consideration, especially when the anatomy of the pulmonary arteries is studied. Indirectly, however, the lymphatic system probably plays an important part in determining the seat of pulmonary tuberculosis, because infectious matter may be introduced with the lymph through the thoracic ducts into the venæ cavæ. It is certain that tubercle bacilli can pass through lymph nodes, since scrofulous infection of distal glands is so frequently succeeded by that of proximal. The fact that scrofulous infection occurs shows that the bacilli can be absorbed by lymphatics through mucous membrane or skin. Whether absorption takes place only through wounds in these surfaces or through normal unbroken tissue is not important. It frequently occurs.

The pulmonary artery arises from the right heart and soon divides into two large trunks the course of each of which is represented by a curve whose convexity is directed upward. The first branches given off from the main trunk supply the upper lobes. These brances arise from the superior surface of the main vessels—*i. e.*, from the convexity of the curve. These branches give rise to others which pursue almost a straight course to the pleural surface. This is true of the larger subdivisions which accompany the larger bronchi. Before arriving at the pleura they give rise to a large number of short vessels whose course is nearly at a right angle to their own. In a paper read at the New York Academy of Medicine some months ago, the writer called attention to the fact that nowhere else in the body does a large arterial trunk give rise to such numerous small branches. Only one more point is of importance for our present purpose. It is that rather larger arterioles break up abruptly into capillaries where they enter the lobules, as has already been remarked.

It is evident that substances introduced into the systemic veins must, if not arrested before reaching the right ventricle, enter the pulmonary artery, and, if not small enough to pass through the pulmonary capillaries, must be arrested somewhere in the lungs. Owing to the relatively large size of the pulmonary arterioles, it is evident that emboli whose diameter is considerably greater than that of the

[1] See "The Anatomy of the Lungs," etc., N. Y. Medical Journal.

capillaries can pass through the whole length of the former vessels and only be arrested at their abrupt termination in the capillary network.

If tubercle bacilli enter the pulmonary arteries, does the anatomy of these vessels suggest a reason for the frequency of tubercular infection of the apices? It seems to me that it does.

The blood circulating in the pulmonary arteries must behave as any fluid does in motion through curved tubes. It is unimportant for our purposes whether the walls of these tubes are elastic or rigid, since we are concerned only with the moving fluid and with emboli suspended in it. The course pursued by such emboli is not much influenced by the elasticity of the vascular walls, but it is greatly influenced by the changes in direction of the moving fluid produced by them.

I hope I may be pardoned for reminding you of certain well-known physical laws. In the first place, as you will remember, a body set in motion tends to continue moving in a straight line, and does so unless influenced by some force whose direction is not the same as that which was first applied. In the second place, momentum is determined by the mass of a moving body multiplied by the speed of its motion. If two bodies move in the same direction at the same speed, the momentum of the heavier will be greater than that of the lighter, and, therefore, the heavier is able to overcome a greater resistance than the lighter.

Let us apply these laws to a fluid in motion through curved tubes and having suspended in it small, freely moving solid particles. The course pursued by these solid particles will vary accordingly as their specific gravity is greater than, equal to, or less than that of the fluid. If the specific gravity of the suspended solid particles is greater than that of the fluid, their momentum will also be greater; therefore less force is required to change the direction of the motion of the fluid than that of the solid particles, and the latter are thrown against the outer—*i. e.*, peripheral—wall of the tube.[1] In the pulmonary artery,

[1] Extremely small emboli are not possessed of momentum sufficient for them to overcome the resistance of the fluid in which they are suspended as quickly as those of larger size. This resistance tends to prevent them from following the same course as the larger, for they cannot as soon reach the outer walls of the curved tubes. On the other hand, emboli of considerable size, though they tend to run along the outer walls, must pursue a different course from both the somewhat smaller and the very smallest,

therefore, small emboli whose specific gravity is greater than that of the blood must tend to approach the upper wall of the two main trunks, since this wall forms the periphery of their curves. The branches supplying the upper lobes arise from this upper wall. Therefore these small emboli would naturally enter them. The course of large emboli must be different, and they would probably enter branches supplying the lower portions of the lungs. It is needless to explain in this paper the reasons for this difference. I would recall to your minds that size is relative.

If small emboli containing tubercle bacilli enter the right heart, and if the specific gravity of such emboli is greater than that of blood, they must be driven far more frequently into the apices than into any other part of the lungs.

If the conditions just mentioned actually obtain, the theory of the infection through the pulmonary arteries is so plausible that it may almost be said to be proved. Unfortunately, however, proof is lacking in regard to two important factors. First, it cannot be positively stated, although it is perfectly conceivable and quite probable, that small masses containing tubercle bacilli ever enter the blood through the thoracic ducts; second, supposing that such masses do enter the blood in the manner stated, it is not proved that their specific gravity is greater than that of the blood. Cheesy matter obtained from scrofulous glands is, in all cases observed by the writer, of higher specific gravity than the blood-serum. As is well known, such matter contains numerous bacilli. If the small infectious emboli find their way into the blood through the lymph-vessels, they probably are composed of cheesy matter containing bacteria. Certainly no emboli capable of passing through the lymph-vessels can be very large, and therefore, so far as their size is concerned, there is no reason why they should not enter the apices. The bloodlessness of tubercle in the lung, the frequency of endarteritis and of areas of coagulation necrosis as accompanying lesions, and the growth of the youngest tubercles near the point where the pulmonary arteriole enters the lobule, are strong evidence that the infection takes place through the pulmonary arteries.

as regards the branches which they enter. These large emboli feel the effect of certain influences which the smaller do not, which result from the viscosity of the fluid and its friction upon the walls of the containing tubes.

Finally, there is no satisfactory evidence to show that it takes place in any other way.

There is much in this paper open to the objection that the statements are perhaps, theoretically, correct, but that no proof is offered of their correctness. It must be said, however, that the paper does not pretend to be anything but a report of the theories based upon investigations of the anatomical and physical questions involved, which seem to the writer plausible and worthy of study. Certain facts are reported which are of considerable importance. Some of the recorded observations are probably new, though this is a matter of no moment. All, new or old, have been demonstrated personally by the writer.

The facts may be summed up as follows:

1. The tubercle bacillus is found far more frequently in the upper than in the lower lobes of the lungs.

2. While the pneumococcus does not so often as the tubercle bacillus lodge in a particular part of the lung, nevertheless, in about four-fifths of all cases of pneumonia the lower lobe of the left lung, or the lower or middle lobe of the right, is the seat of the disease.

3. Inhaled dust does not usually lodge first in the part of the lungs where the tubercle bacillus is found.

4. It is impossible to drive any fine powder into the air-vesicles after the lungs have been removed from the body, positive pressure being employed.

5. The tubercular process involves the walls of the vesicles before the bronchi are affected, at least in a vast majority of cases.

6. Neither liquids nor solids in the bronchi are more often found in the upper than in the lower lungs. In bronchitis, acute or chronic, the secretion is found in the bronchial tubes proper, and not in the air-vesicles, and it is no more abundant in one lobe than in the others. In cases of hæmoptysis the blood rarely finds its way into the vesicles, and the particular set of tubes which contain the greatest amount of it is determined by the original seat of hemorrhage, the quantity of blood, the rapidity and duration of its flow, and the position of the patient. When the hemorrhage is so profuse as to expel most of the air from the larger tubes, as is the case when, for example, an aneurism of the aorta ruptures into the trachea, or a large branch of the pulmonary artery is the source of the hemorrhage, the blood fills the vesicles, but this occurs as a result, not of the movements of respiration,

but of the pressure of the effused blood propelled by the heart. This has no bearing upon the subject under discussion.

7. There is no evidence that the movements of the thorax affect any part of the lungs more or less in proportion to its bulk than any other part.

8. Among civilized people there is a marked difference between the sexes in the type of breathing. Women do not suffer from consumption quite so frequently as men; but consumption in women begins at the apices in about as many cases of consumptive women as it does in consumptive men.

9. The pulmonary artery and its main branches describe curves whose convexity is directed upward. The bloodvessels supplying the upper lobes are given off from the convex surface of the main trunks.

10. Small particles immersed in rapidly moving fluid, when passing through curved tubes, are thrown against the outer wall of the tubes if the specific gravity of the particles is greater than that of the fluid. In the pulmonary arteries small emboli of greater specific gravity than the blood would tend to run along the upper side of the main branches and enter the trunks which supply the apices. If the particles are extremely small, or if they are large enough to occupy a considerable part of the calibre of the tube, this tendency is not so marked as it is in the case of particles whose size is sufficiently great for them to attain a momentum capable of overcoming the friction which the surrounding fluid exercises upon them, yet not great enough for them to be affected by the direct force of the current.

11. The contents of the lymphatics enter the venous blood through the thoracic ducts.

12. Tubercle bacilli can, and often do, pass through lymph nodes.

13. Cheesy matter is heavier than blood serum.

The following statements are probably correct, but are not proved:

1. Tubercle seems to begin at the points where the pulmonary arterioles give rise to the capillary network.

2. Small masses of tubercle bacilli seem to have a greater specific gravity than blood serum. (Such masses grown upon beef-peptone-agar were found by the writer to sink in a solution of common salt after the agar had been thoroughly washed off. The experiments were too few in number to be regarded as conclusive.)

The foregoing statements make it probable that the infectious

material producing consumption enters the system and is conveyed to the apices of the lungs, not by direct inhalation through the bronchi into the air-vesicles, but that it is absorbed by the lymphatics or blood-vessels, and, passing through the vena cava and right heart, it is swept along the upper wall of the right or left pulmonary artery and, entering the branches which supply the corresponding apex, is arrested by the capillary network. It is probable that the virus is introduced much more frequently through the lymphatics than through the bloodvessels. There is abundant evidence to show that the mucous membrane of the mouth, nose, and pharynx permits absorption of the bacilli through its lymph channels. The fact that lymph nodes do not, in other parts of the body, completely prevent the bacteria from passing, makes it extremely probable that the lymphatics of the stomach and intestines also permit them to pass. The mucous membrane of the trachea and larger bronchi may very possibly become infected, but it is through their lymphatics that the bacilli are introduced and follow the same course through the thoracic ducts, right heart, and pulmonary artery, as bacilli do, when absorbed through other mucous membranes.

Whether true or false, this theory is sufficiently plausible to make us careful not only to prevent the inhalation of dried sputum containing bacilli, but also to guard against its introduction into the system through the mouth, nose, stomach, intestines, or wounds in the skin. The handling of any receptacles containing the sputum of a consumptive might be the means of subsequent infection through the nose or mouth. The milk of tuberculous cows is dangerous not only because it may occasionally produce general tuberculosis, but also because it often causes pulmonary tuberculosis, the bacilli passing through the thoracic duct and being arrested in the lungs. Tuberculous meat may in a similar manner produce consumption. The possibility of bacteria being introduced by any food upon which they have chanced to lodge should not be forgotten. It is not at all unlikely that the dust of dried sputum may infect salad, cold meat, or previously untainted milk.

In conclusion, I wish to say that I am not advocating any preposterous efforts to avoid tubercular infection. I do not wish every one to eschew salads, cold meats, unboiled milk, etc. Two things must be borne in mind: First, that, although about one-seventh of all human beings die of tubercular diseases, six-sevenths do not, and

of the six-sevenths probably nearly one-half at some period of their lives suffer from pulmonary tuberculosis and recover from it. Second, that to produce fatal tuberculosis the quantity of bacteria introduced must be very great, and the individual who absorbs them must be in a condition which makes it possible for them to live in his body. Anyone who has inherited or acquired what is called a tendency to consumption should take particular pains, first, to improve the general condition of his body, and then to avoid every possible source of infection, whether by food or anything else. The clothing of consumptive people should be regarded as dangerous to handle. Burning a certain amount of phthisical sputum is not a sufficient means of preventing the spread of the disease. Doubtless many bacilli are destroyed if the sputum is burnt—as the only good bacillus is a dead bacillus—but a great many may never get into the receptacle provided for them, but may lodge upon some portion of the clothing of the patient. Every article of clothing used by a consumptive is a possible source of danger to other vulnerable people who come in contact with it.

Life would not be worth living should we undertake to avoid every conceivable chance of infection by microbes. "Three score years and ten" of life spent in shunning human society, either on a high plateau or a desert island where the germ of malaria is unknown, drinking distilled water, avoiding uncooked and eating only overdone food, would be an existence not altogether without certain drawbacks to the majority of people. Even these precautions might not insure immunity. A certain amount of risk must be taken by everyone who wishes to do anything with his life. It is possible to spend so much time in prolonging one's existence as to make that existence both useless and unendurable. It is, however, worth while to study every possible source of tubercular infection, since by this means some lives may be saved.

Killing tubercle bacilli seems a rather futile occupation. Though a hundred million were destroyed every day, countless billions would survive. If the entire human race should unite to exterminate them, it is doubtful whether it would succeed. This, however, is no reason for neglecting to disinfect everything which we know or believe to harbor them.

The story of the gentleman who lived in a country infested by

venomous snakes is appropriate. He stated that for twenty years he had killed at least twenty snakes daily, but that the killing of one hundred and fifty thousand, more or less, seemed not at all to have reduced their number. When asked why he continued his hopeless fight, he replied that "he still objected to them as much as ever in the parlor."

DISCUSSION.

DR. WELCH: I wish to express my appreciation of the great value of the experimental and anatomical work relating to the lungs which has been performed by Dr. Roosevelt. The most important part of his paper, which embodies only a small part of his original work, appears to me to consist in the experimental proof that small particles when inhaled go only a comparatively short distance into the bronchi, and that the mechanical and other conditions usually assigned for the assumed frequency of penetration of tubercle bacilli along the air-passages into the apices of the lungs, are either not operative or do not exist at all. He has not only criticised acutely the current theories on this subject, but has brought forward direct experimental evidence against them, and this is to be welcomed as a genuine and important contribution to our knowledge.

His suggestion that we may perhaps better explain the common localization of tuberculosis at the apex by assuming that the bacilli are conveyed there by the blood-current rather than by the air-passages, seems to me open to serious objections. He has himself pointed out the manifest difficulties which this hypothesis meets in the known behavior of emboli carried to the lungs by the blood circulation. It matters not whether these emboli be large or small, heavy or light, portions of thrombi or tubercle bacilli detached from a tuberculous thrombus in the thoracic duct, there is evidence from post-mortem observations on human beings that they have no preference for lodgment in the apices of the lungs.

There is a point of view to which Dr. Roosevelt does not seem to have attached sufficient weight. In order to explain the more frequent occurrence of pulmonary tuberculosis at the apex, is it necessary to demonstrate that tubercle bacilli are more frequently carried there than to any other part of the lung? May we not equally well assume that even if the bacilli are conveyed no more frequently, or possibly less frequently, to the apex, that they find there especially favorable conditions for their invasion and growth, whereas under ordinary circumstances they do not find similar conditions when they enter other parts of the lungs?

DR. WILLIAM M. ORD, of London: I desire to endorse Dr. Welch's criticisms. While I admire the ingenuity of the attack and its conclusive-

ness, the constructive part of the paper appears to me defective. The arguments Dr. Welch has used had already commended themselves to me. In fact, I have long thought, myself, that the deposit or the formation of tubercular deposit in connection with bacilli at the apex of the lung, has been chiefly determined by a selective power existing in that part of the lung, a selective power offering in some way increased facility either for the deposit or for the further development of the bacillus—the preparation of a suitable nidus.

You will say that this idea would involve some indication, that we can find in an anatomical way, of weakness proper to that part of the lung. That, I think, we have done to a certain extent. The apex is much more prone to smaller localized inflammations—to that kind of process in which we know that tubercular bacilli readily find a nidus for their development.

I am always reminded, in thinking over this matter, of some teachings of the late Sir William Gull. He used to say, take a python's lung: it is a long bag, the upper part of it having very little vascular and no vesicular development. Lower down we begin to find a network of miniature alveoli and larger alveoli extending to a central cavity. Lower down at the extreme base of the lung we find a fully developed lobular tissue. One may find the same thing in the batrachians and even in the higher oviparous vertebrata, such as the duck. Sections of the lung, when looked at, show that there is not as good organization in the apical as in the basical portion. I am inclined to believe that such difference is more marked in early development. I should suggest that we must recognize that there is some kind of relative want of resisting power in this part of the lung. But whether or not we can find in comparative anatomy some explanation for this, it has always seemed to me of considerable interest.

DR. VAUGHAN: I wish to emphasize the criticism made by Dr. Welch. It is exactly those cases which result from inoculation through the blood and lymph which are not localized in the apices. This is borne out both experimentally and clinically. In experimentally introducing tuberculosis by way of the intestinal canal, the tuberculosis is in the mesentery and in the intestines; or, if in the lungs, not specially localized in the apices. So much for experimental evidence. Clinically, tubercular disease of children from three to eight years of age, as was admirably pointed out by Dr. Burdon Sanderson, is mostly of the intestines and mesentery and is not located in the lungs; or, if so, there is no especial localization in the apices. Then, again, when we inject cultures of the bacillis tuberculosis into the blood, according to the view of Dr. Roosevelt we ought to get special localization in the apices. We do not. As Dr. Welch says, we are likely to get miliary tuberculosis. It seems to me that the weight of the evidence, experimental and clinical, is against the theory of Dr. Roosevelt. I certainly agree with him in the criticisms he has made of other theories, but I should hesitate very much in accepting that which he offers.

DR. JACOBI: I mean to offer a suggestion only. The suggestion is, that the gentlemen who try to find out why tuberculosis localizes in certain spots, do not spend all their efforts on healthy lungs but experiment also on diseased lungs, for tuberculosis, as a rule, will not affect a healthy lung.

At first I will express my opinion that in all probability those cases of tuberculosis which are the result of embolism, unless they be miliary, are very probably rare compared with those which are the direct results of the location of the bacillus on and in the mucous membrane. It is the same thing with all infectious diseases. Compare, for instance—that unfortunately so well-known instance—diphtheria. As long as the mucous membrane is healthy you have no invasion of diphtheria. There may be ever so much diphtheria about—a whole epidemic—and the individual case will not occur unless the mucous membrane of the nose, of the pharynx, or vagina, is the seat of a previous catarrh, with the exception of those very few cases in which diphtheria locates in the tonsils in the apertures between the epithelia as shown by Stoehr. In order to have an invasion you must have a diseased mucous membrane; you must, at least, have a catarrh, you must have an abnormal condition of the epithelium—the epithelium tumid or removed altogether, or changed in some way or other. It is the same way in tuberculosis undoubtedly. We speak of the necessity of a predisposition to tuberculosis if the disease is to occur in an individual, for certainly cases of congenital tuberculosis are so very rare that I have claimed lately that there is only one genuine case on record. What does that predisposition mean? Predisposition means an insufficiently developed chest, no matter whether it is arrest of development or whether it is premature ossification of the ribs, sternum, etc. But we always claim that there must be a predisposition; mostly under the influence of heredity. We speak of "weakness of the tissue," and I believe when we cut it down to its proper proportions this "weakness of the tissue" means an abnormal circulation or an improper condition of the epithelium.

Now, when I said I would like to direct the attention of those given to these researches, to the abnormal lung, I would say that I wish them to find out why it is that the bronchi and bronchioles of the upper part of the lung —the apices—are so much more given to abnormal conditions. Why I ask that question is perhaps explained best by the fact (or what I look upon as a fact, because I have seen it hundreds and hundreds of times) that in most cases of extensive tuberculosis in the young you find cavities at least just as many times, and, I think, in the great majority of cases, in the lower lobes. Why? Because the lobular pneumonias and lobular catarrhs take place more frequently in the lower lobes, and not unfrequently bilaterally in the lower lobes than anywhere else in the lung; and it is here that I have found cavities most frequently. I believe that the tuberculosis was deposited there because the lungs were in the condition best adapted to the reception of bacillary invasion. There was broken-down epithelium and the bacilli could get deposited there and were not to be expelled by the fimbriated epi-

thelium. Thus the question arises, Is it true or probable that there is an abnormal condition of the epithelium in the apices of the lungs of the adult similar to what is so frequently found in the lower lobes in the very young? This is only a suggestion, and is offered as such and nothing else.

There is one thing which may be studied at the same time: Why is it (and it is certainly a fact) that the cases of chronic interstitial pneumonia are more freqnently found in the upper lobes than in the lower? From what I have seen in many years, it is certainly a fact that interstitial pneumonia, with proliferation of connective tissue and afterward cicatrization and retraction and bronchiectasis, is found in the upper lobe more frequently. I believe there must be some connection between that fact and the other fact. There is very probably a condition of the circulation which, at the same time, is a cause of the deciduous condition of the epithelium and also of the proliferation of cellular tissue. But this is a secondary suggestion. The first one, I believe, is perhaps more important. If the matter is studied from the point of abnormal rather than from normal lungs, I believe we will come to some conclusions.

DR. ROOSEVELT: I know that the work of destruction is much more easy than that of construction, yet it is worth while to attack all theories, for if they are demolished they must be false and misleading. It is impossible to destroy them if they are true. Construction of a correct theory is difficult; but destruction of such a one impossible. The theory which forms such a prominent part of this paper is not advanced by me as proven. It seems plausible, in spite of the perfectly just objections advanced by Dr. Welch. The conditions to which I refer do not resemble those which obtain when an enormous number of bacilli are continually being poured into the blood from a tuberculous thoracic duct, or when a blood-clot large enough to occlude a large branch of the pulmonary artery is concerned. Hemorrhagic infarcts seem to me more often to be the result of thrombosis than embolism.

The question of local vulnerability as determining a soil suitable for bacillary growth is not considered in this paper. It is something so vague and intangible that I wished, if possible, to ascertain whether some physical explanation could not be discovered which would be more comprehensible.

The most important point in the paper is to establish the fact that inhalation does not account for the phenomenon. This is a matter of practical value, for it makes it the more important to appreciate the risk of tubercular infection in other ways than through the air.

ON CERTAIN ARRANGEMENTS MADE IN THE CITY OF GLASGOW, 1866, WITH A VIEW TO THE PREVENTION OF EPIDEMIC CHOLERA.

With an Appendix.

By W. T. GAIRDNER, M.D., LL.D.,
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF GLASGOW, SCOTLAND.

I believe I shall not detain you very long in this, almost *ex tempore*, address or paper (if paper it may be called), because you will very speedily discover that it is not a paper, but only the materials out of which a more or less elaborate paper might have been built had the opportunity occurred.

When conversing with your President, Dr. William Pepper, at Newport, since my arrival and only some days in advance of this Congress, it seemed to be worth while considering whether certain experiences which had occurred to me during the last threatened invasion of cholera in Glasgow during the autumn of 1866 could be presented verbally, or on the basis of brief notes, without details of facts or documents, so as to be a suitable communication for this Congress. Dr. Pepper has ruled that it is to be so; and here I am, accordingly, not to read a paper, but to make a short statement, which, from the very nature of these circumstances, must be as concise and as much detached from documentary details, facts, and statistics as I can possibly make it. And yet I think that even this bare statement of my experiences as the Medical Health Officer of the city of Glasgow in 1866 cannot fail to have a certain interest for you.

America, to us of the old country, is the land of experiments, political, social, religious, educational, and sanitary; yet it does not appear to me that I have ever heard of anything, either on your

vast continent or in my own little island of populous places, precisely on the lines of what I am now about to narrate. The practical issue before my mind is whether out of this experience I can place before you any considerations of importance applying, of course, with variations founded on local differences, to any circumstances arising or likely to arise in the midst of your complex and ever-extending civilization. If I shall have the good fortune of exciting or stimulating one fruitful idea, one speculation which can be carried forward into action in this wide continent, my task will have been accomplished, because the good seed will have fallen into good ground, and will in time bring forth its results. I may add that my own opportunities of initiation in such matters may be said to be over, and I have, therefore, no personal, nor even any official, object to be gained or lost by this paper.

On going from Edinburgh to Glasgow, in 1862, as Professor of Medicine in the University, the position was offered to me—almost, indeed, forced upon me by the authorities—of the medical chief of the Sanitary Administration, then about to be recast at the instance of Mr. John Ure, a most devoted sanitarian, and afterward Lord Provost, or chief magistrate of the city. This position I held for nearly ten years, and then resigned it, being succeeded by my good friend, Dr. J. B. Russell, known, I am certain, by reputation to many of you, as he is to us all over Great Britain, as one of the most diligent, most active-minded, most original, and withal most trustworthy of public medical officers; and if I have still any legitimate pride in having held that office for a few years from its commencement, it is in having laid some of the first foundations for a superstructure which has, under his admirable superintendence, become almost a model of civic sanitary administration. Still the precise conditions of the experiment I have now to relate have not chanced to recur during the period of Dr. Russell's tenure of office, nor are the administrative means and machinery at disposal now precisely what they were in 1866. So far as my information extends, therefore, the experience I have now to record is, as regards its method and its mechanism in some respects, absolutely unique.

Typhus fever, our ever-present, ever-watchful plague in Glasgow, and in all our cities inhabited largely by dense Irish populations,

was, at the time I speak of, so much of a home pestilence that it had ceased to be regarded as anything extraordinary, even when represented by hundreds, not to say thousands, of cases. It was held, in fact, by the legal advisers of the local authority that exceptional measures could not legally be taken against typhus fever until the hundreds had *become* thousands; that, in fact, it was not legally within our competency to "shut the stable door" effectually until, as the proverb says, "the steed was stolen." This was the main defect of the local Sanitary Act under which the administration had to be conducted in 1866; and it is necessary thus to emphasize it, because it may just be possible that in some of your various States and Territories a similar defect may still hamper the work of your medical officers; and at all events it is the contrast to this state of matters, as arising from the widespread apprehension of cholera and the comparative ease of getting power to do things more thoroughly, that will give the key-note, as it were, to the present address. I desire, however, to add, as the necessary sequel of what has now been set forth, that the defect alluded to has long ceased to exist in Glasgow; indeed, it only required the experience of a very few years to show that it was a bad and utterly false economy to build hospitals and institute sanitary works of disinfection, etc., upon a temporary plan, and as if intended only for an epidemic emergency, specially declared to be such.

In August, 1865, however, it became my duty to report to the Lord Provost and magistrates as regards a circular letter addressed to the heads of our municipalities generally, by the Secretary of the Privy Council, "referring to the recent appearance of cholera in Egypt and the occurrence of some cases in Turkey and in Italy;" the object of the communication being, as stated, "that the authorities of your locality may be enabled to take such steps as they think proper for the preservation of the health of the inhabitants of their neighborhood." I will not detail here the proceedings which more immediately followed from this warning-note of the Privy Council; the only point on which I wish now to insist is that it placed the probable advent of that disease so clearly and definitely before the authorities and the citizens generally as to constitute an exceptional case of apprehended epidemic disease, and thus to set in motion at once the provisions under the local Act of

Parliament for dealing with such exceptional cases.[1] While, therefore, it absolutely required a new and a much stronger Act of Parliament, or rather more than one such Act, to clear the way, even for dealing effectually with what was regarded as a home-bred pestilence, in the case of typhus fever, the medical officer and staff found themselves at once invested, as regards cholera, with almost autocratic powers, limited only by the consent of the magistrates, which, as it happened, was in this instance easily obtained, and in thorough accord at the time with public opinion.

In the latter part of 1865, as the result of the powers thus obtained, numerous measures of general sanitary improvement were urged on, to which it is not necessary now to allude, because in any case they would have had to be undertaken, sooner or later, though possibly not considered as urgent. One of these was a detailed examination and report on all the public wells to be discovered within the bounds of the local authority; these being by no means numerous, as they had mostly been superseded long before by the excellent supplies from Loch Katrine and elsewhere, furnishing to the inhabitants a mean quantity of fifty gallons per day for each individual of the population, and this of the purest water, perhaps, ever distributed to any municipality in the world. The Loch Katrine water-supply was introduced in 1859; my concern, therefore, was not with the supply, but with its distribution. In order to obtain the full advantages of a thoroughly good water, and to remove the temptations to use for drinking any less perfect sources of supply, it was necessary in some cases to suppress the latter altogether, replacing them by the Loch Katrine water; or, in other cases where no evil appeared likely to result, leaving one, possibly less pure, supply open for washing or bathing, while the Loch Katrine water was abundantly distributed for drinking purposes. But on these details, though interesting enough in themselves, I do not intend to dwell at present. My own belief, from first to last, was that the Loch Katrine water would prove, at least in a com-

[1] The precise legal import of the remark above, under the provisions of the local Act then in force, was that by a certain form of declaration, published in the newspapers by the medical officer, sections of the Act were brought into operation, at the instance of the Lord Provost and magistrates directly, without undergoing consideration or criticism by the board of police, which, at the time referred to, was the sanitary local authority for all ordinary occasions.

parative sense, the salvation of Glasgow from the worst ravages of Asiatic cholera; and this anticipation was fully justified by the result.

But we had to do with a vast population, largely composed of the operative classes, and in by far too large a proportion composed of those classes with whom the crowding of a whole household, and perhaps a lodger or two, into one apartment, represents the average condition of domestic comfort. Moreover, this large mass of wretchedly housed persons was also densely packed upon a ground-space smaller in reference to the numbers of population than in any city of Great Britain and Ireland, with the single exception of Liverpool. In some parts of Glasgow it was the case at this time that nearly a thousand persons lived upon a superficial acre of ground. The habits of these people were, of course, often extremely filthy, and even the possibility of cleanliness was too often denied to them by the faults of construction in their enormous tenement-houses, without any proper lavatory arrangements, or even distribution of water, and very often without anything like suitable means of getting rid of the discharges. All these faults, moreover, were, as it were, ingrained; not only expressed in the habits of the existing generation, but inherited from their predecessors, in so much that I had had occasion to point out that not only epidemic disease, commonly so-called, but also tubercular diseases, pneumonia, bronchitis and respiratory diseases generally, and, above all, an enormous death-rate of very young children, marked these densely occupied portions of the city to a degree many times greater than was the case in the more privileged and happily placed portions of the community. Such measures as had been considered possible up to this date, in the face of a rising epidemic of typhus fever (nearly at its height in 1865–66), were chiefly police regulations as regards gross overcrowding, hospitals for the sick, arrangements for ambulances, etc., disinfection of rooms and of clothing, and, in some cases, the compulsory clearance of whole tenements so as to permit of the removal temporarily both of the infected and non-infected inmates, and the more complete use of the means of disinfection.

All this, although it cost us all much time and forethought, and the city considerable annual expenditure, was done; and yet I had

the habit of expressing myself freely to the effect that we were only "scratching the surface"—that is to say, that to meet fully and adequately the abiding causes of typhus fever in our midst, it would be necessary to obtain greatly increased powers, and use them largely for the destruction, and perhaps reconstruction, of certain localities. These powers were finally obtained in a local Act of Parliament, called the "Glasgow City Improvement Act," for the promotion of which we were chiefly indebted to Mr. John Blackie, then Lord Provost, and the late Mr. John Carrick, city architect, one of the most admirable of officials, whose sure instinct, amounting to something like genius, but founded on practical experience and guided at once by wisdom as to the end to be achieved and knowledge of men as to the means to be used, was of inestimable service. All this is now a matter of history, and I do not mean to detain you upon it, my object being merely to indicate to you the state of the population on which the cholera was expected to fall in 1866, before any of these greater reforms to which I have alluded had been even initiated, much less carried out, as they have been since, under Dr. Russell's tenure of office, with excellent results which he has officially demonstrated.[1]

Now, gentlemen, with all the confidence I then had, and, as it now appears, justly entertained, of the probable effect of a pure water-supply as a protection against the worst epidemic excesses of Asiatic cholera, it was impossible to observe from day to day and from week to week, this terrible disease drawing nearer to us in Europe, and finally in England, without a vast and indefinite sense of responsibility and of possible disaster. It had been amply shown in 1848, and still more clearly in 1854, that places which had obtained a purer water-supply suffered notably less, and, conversely, that other places in which the water-supply had deteriorated, suffered more in the later than in the earlier epidemics. But with all the hopes which could be founded on this recorded experience, it was impossible not to fear that a population such as ours then was, already decimated by epidemic disease, and living too often in the most grossly insanitary circumstances, having, moreover, at all times a very much higher death-rate overhead than any other city

[1] "Results of the City Improvement Act," by J. B. Russell, M.D. (In the Transactions of the Glasgow Philosophical Society.)

of the United Kingdom except Liverpool, might still be heavily hit, as it were, in accidental localities by the epidemic that was looked on as now bound to come.

In all the past epidemics of cholera, Glasgow had suffered severely, in some of them most severely, and not least in the epidemic of 1854, the one immediately preceding. It was, therefore, with no ordinary solicitude that we proceeded in the early months of 1866 to make such arrangements as might be found most suitable for protecting our only too vulnerable masses of dense population from a scourge in regard to which imagination might possibly, indeed, outrun the reality, but for every avoidable case of which, actually occurring, we could not fail to hold ourselves in a measure responsible. I am happy to say that the Lord Provost and magistrates, as well as the citizens generally, were all of one mind in this matter. There was no mere unmanly sense of panic, but all arrangements in advance were left to the authorities, and the medical officer had therefore, speaking practically, a "free hand."

The first thing that occupied us, apart from those early precautionary measures to which I have already referred, was the question of hospitals for the sick. With a view to typhus fever and other epidemics, a considerable amount of hospital accommodation had been already provided by the local authority, in addition to the Royal Infirmary and the hospitals of the several parishes, which were administered by separate boards of managers, and supported either by parochial assessments, or by the voluntary liberality of the citizens and others.

It was determined, under the circumstances, to request the several parishes to undertake the hospital accommodation for fever and all other epidemics except cholera, *pro tempore*, so that the hospital of the local authority might be cleared, and held open for cholera cases exclusively, so long as it might be required. Dr. Russell, who had even at this time won the confidence of all as the medical superintendent of the epidemic hospitals of the local authority, was appointed to deal with the details of this department, to engage a staff of nurses, etc., and to obtain all the furnishings and equipments for such hospitals as might be under the control of the local authority temporarily during the cholera epidemic. Ultimately, one other temporary hospital was built and fully furnished in ad-

vance, in a very central situation, and provision was made as regards sites, etc., for four others; but of these only the hospital in Glasgow Green was actually brought into use, and this only for a few weeks during the incidence of the epidemic.[1]

I may mention, in passing, that the enrolment of suitable nurses proved a work of the utmost difficulty, involving almost heart-breaking disappointments in detail, from the great number of applications from persons morally or otherwise wholly unsuitable, and the small number available who could in any way be relied upon. Had the epidemic proved much more severe, this would have been one of our greatest difficulties, but it was surmounted by the patience and foresight of Dr. Russell.

The next point was the arrangement, in advance, of a medical staff. In this, happily, no serious difficulty was encountered, either on the side of the authorities or of the medical men in practice. In a very short time the medical officer was enabled to submit arrangements as to remuneration, etc., which gave general satisfaction, and about eighty of the fully qualified medical practitioners of the city, many of them having had previous experience, and all of unquestionable status, were enrolled as willing to undertake the treatment of cases of choleraic disease at the instance of medical or other visitors, or of the local authority. As it was anticipated, however, that in the event of serious panic, or of even trivial diarrhœal disease occurring in a locality, there might be an undue amount of disturbance, or even unnecessary calls upon this medical staff, especially during the night, it was determined to interpose a staff of house-to-house visitors, not necessarily qualified medical practitioners (though having sufficient medical information to deal with ordinary or false alarms), between the strictly medical staff in the infected districts and the general population. The precedent here followed was that of previous epidemics in Great Britain, in which the principle of house-to-house visitation had been always found to

[1] It was placed under the medical care of Dr. James Adams, whose great experience in former epidemics was thus turned to account, Dr. Russell himself taking medical charge of the hospital in Parliamentary Road, already alluded to. The nursing staff was arranged so as to be common to both hospitals (as it would have been also to the others had they been required), and to be detailed by Dr. Russell for service where most urgently wanted. The kitchen arrangements and the disinfecting staff, as also the supply of beds, bedding, etc., was also managed for the Parliamentary Road.

be of great service in ascertaining and dealing with the premonitions of the choleraic attack.

Closely associated with these arrangements was the opening of dispensaries, or depots for medicines and disinfectants, to be open day and night during the whole period of an apprehended epidemic, in all quarters of the city. Here, too, as in the case of the medical staff, no serious difficulty occurred. The machinery was, in fact, already provided, partly by the shops of the chemists and druggists, and partly by the surgeries of the medical practitioners. It was necessary only to secure a constant day-and-night service in a certain number of these, selected with a view to convenient access in all parts of the town, and to furnish them with all the remedies and disinfectant substances recommended by the authorities, as also with a uniform series of printed labels, boxes, and bottles for giving out daily supplies of disinfectants for use, on application, so as to save at once time and expense, and to secure as far as possible uniform quality in the leading articles dispensed. In addition, these depots were to be used as houses of call, where information might be given of cases either of real or of apprehended choleraic or diarrhœal disease; where also medical assistance could be at once secured, if necessary, or the services of the official disinfectors could be called into requisition, or house-to-house visitation could be organized, so far as immediately required in case of first alarms. The name and address of several of these depots was to be placed at the disposal of each household, in a manner presently to be described.

I need hardly add to the above, that the whole of the ordinary cleansing and disinfecting staff, as existing permanently in connection with the sanitary office and cleansing department, required to be largely reinforced, even long in advance of the first indication of a local epidemic; for the instructions of the Privy Council, already alluded to, in August, 1865, had brought the subject of much more thorough cleansing before the authorities all over the kingdom, and reports were daily transmitted, both to the cleansing department and to the office of the master of works, involving a great amount of additional work, which went on increasing in proportion as the attention of the citizens was drawn to the subject, on the one hand by the gradual approach of the epidemic and on

the other by the invitations of the medical officer to make known any obvious cases of defect or neglect. The provision of disinfectants on a large scale and on the most approved principles then ascertained, was entrusted to the cleansing department, which also undertook to furnish the depots above named.

But when all this, and more, had been done or arranged for, the problem was still ever pressing on my mind, How to get the practical knowledge of what had been and was being done for their protection brought home effectually to the minds of the people chiefly concerned. This was a very serious matter, perhaps the most serious matter of all. There were at this time nearly 100,000 separate households or about 500,000 inhabitants in what was officially reckoned as "Glasgow," being under one municipal government as such. Many of these households, as we had had ample and sad experience, were living in a state of almost brutish ignorance and neglect. Epidemic disease generally had almost no effect on the daily lives of such people—it was taken as a thing of course, and met, if with any emotions at all, with a kind of sullen, blank fatalism and despair. A new and to most of us a terrible epidemic disease might produce the same effect or want of effect; or, on the other hand, it might lead to an unreasoning panic, always the most unprofitable and even disastrous of mental states; because no fruitful action ever arises or can arise out of mere selfish cowardice. The thing to be done, therefore, as it appeared to me at this time, was to get at the heads of these separate households or at least at some of the members of them, by personal and direct communications, so as to press home to their convictions by the best simple arguments that could be devised, what was being done for them and what, on the other hand, they might reasonably be expected to do—indeed in some cases could only do—for themselves. Without this, it seemed not unlikely that the whole arrangements might break down at the very point where interference was required. Suppose, for instance, that an imported case of the genuine Oriental cholera, or of diarrhœa tending in that direction, was brought into one of these households—how were we officials to hear of it? Possibly through the sudden death of the patient and a sudden frenzy of alarm paralyzing all combined and effective action for good. Possibly, on the other hand, not at all,

or only after quite a number of cases of choleraic diarrhœa, not fatal but dangerous and scattering infection everywhere, had succeeded in arousing the slumbering sense of fear. It appeared to me that there was or ought to be a better way than either of these: but I was not quite clear as to what was the better way, especially as time was pressing and the object was rather to anticipate than merely to meet the advent of the disease which had already been heard of in several of our towns, both in England and Scotland.

When in this state of mind, I chanced to encounter a much-respected clergyman of one of our Presbyterian denominations, and I opened my mind to him on the subject. I asked if he could suggest to me how to obtain *at once* some hundreds of willing and intelligent workers, not necessarily with much medical or physiological knowledge, but broad-minded and sympathetic, who would personally visit and carry medical instructions about cholera down into the homes of the poor—it being understood that if cholera or anything like it should actually appear in any district or block of houses, these volunteers would be replaced at once by medical visitors. His answer was unhesitating and it was in the form of a question; "Why not apply to the churches? they will do it and give you all the volunteers you want, only for the love of God." The reply was exactly on the line of my own thought, but I ventured to remark that I, as a public officer, could make no distinctions among the churches. "Ask them *all*," he replied; "on that point, at least, they ought all to combine and I believe they will do it."

Acting on this hint, I wrote a circular letter in the character of medical officer of the city, pointing out what had been done and what had still yet to be done, and I called upon all the churches indifferently, in which worship took place on Sundays in Glasgow (over three hundred in number), to assist in this work, by sending a deputation of their office-bearers to meet me in the City Hall at a certain date. The idea spread and was rapidly taken up—at the meeting in question nearly all the churches were represented and undertook to furnish me, on an average, with (say) ten picked men each. I said that as medical officer I would be responsible for the disposal of these hastily gathered forces, it being understood that

while suggestions would be received very willingly as to one or other district being taken up as matter of convenience by particular churches, I must in the end be able to dispose of the volunteers absolutely without fear, favor or partiality, and that they must needs all work on one and the same plan. For this purpose I had the whole city divided; first, into seven or eight considerable districts, and these again into minor subdivisions, no account being taken of church districts in doing so. In the ultimate subdivisions the enumerator's divisions at the last census were brought into operation; and finally, a series of maps were carefully prepared on the largest Ordnance scale of twenty-five inches to the mile, by which (within certain limits of difference) a certain proportion of families living in a particular close, or wynd, or row, or street could be assigned to one visitor, who from the section of the map sent to him could not fail to know exactly the limits assigned to him in his visits. While this work was in progress, the churches had their own meetings in many of the larger districts and were maturing their own plans. The enthusiasm in the work was very considerable and increased with its progress.

The first quite definite proposals came from the western district, at the instance of two of the most respected clergymen in Glasgow, Dr. Marshall Lang, then of Anderston Established Church, and the late Dr. Somerville (well-known since then as a foreign traveller and missionary on behalf of his church), of the Free Presbyterian Church in Anderston. These two reverend gentlemen had no difficulty of course in carrying with them the whole of the Presbyterians and other allied denominations, but I thought it of importance to remark at the outset, that from my point of view as medical officer, we must also have the Roman Catholics and the Unitarians, and indeed all others willing to contribute; and that there must be no distinctions. This being fully assented to, the western district was at once set to work and in a few weeks the map (above alluded to) of each coöperator's district was in his hands, with a paper of instructions which he was understood to make the basis of his work, and as such, to carry down to his district (Appendix No. I.). A little later the enthusiasm spread and the other districts came in; it being understood from the first that if the poorer congregations, from having fewer persons of sufficient

independence and leisure, were in danger of being under-manned as regards their quota, the more wealthy congregations should be asked to furnish more visitors in proportion. In the end, 3000 to 4000 intelligent and active visitors had their instructions and were actively at work in their various sections, informing the people and reporting to us at the sanitary office, or to the cleansing, or the master of works' department.

The effect of this great movement, both immediate and ultimate, was very remarkable. In the first place, it was universally felt that the apprehended epidemic of cholera had been provided against in a way that entirely removed local and increasing panic. The feeling of a common interest and of united and sympathetic action in view of a common danger pervaded all classes of the community, and led to a reliance upon the means provided which could not, I think, have been attained in any other conceivable way. The public were so pleased with the hospital accommodation provided by the authorities, that on their being admitted to view the new temporary hospital, all the objections which had been urged against it, as occupying a portion of "the people's park," were at once tranquillized. The feelings of satisfaction with the arrangements adopted for the limitation of the area of disease, and the medical and other regulations set forth, both as regards prevention and treatment, made it clear to the most unreasoning and the most ignorant that their safety lay in the early and an unreserved communication with the authorities. There was no panic, and no disposition either to conceal or to exaggerate individual cases of diarrhœal disease. Everything that was done was done quietly, without undue notoriety and at the same time without omitting any just precaution. And the ultimate result was that Glasgow, with its teeming and badly situated population of the industrial and often pauperized classes, was able, after the epidemic had passed, to show a death-rate from cholera very much less than that of any large town in Scotland, except Paisley, which had from the first adopted somewhat similar precautions. About sixty-six cases of true cholera and a few hundred of choleraic diarrhœa were all that were contributed by a great city of half a million of inhabitants to the sum of this epidemic in Scotland. And the whole of the visitors from the churches concurred in affirming that their work during

the period of apprehension, as above described, had been fraught with inestimable advantages to themselves as well as to the poorer population, by bringing them into actual contact with the condition of existence prevailing among thousands of their neighbors.

One point of detail still demands notice, as bearing on the first cases reported. Several of these were imported cases, and therefore isolated, but, of course, carefully watched for in the first instance. It appeared probable that the various newspapers, seeking on all hands to obtain the first intelligence of the epidemic as advancing from Liverpool and other cities having communications with Glasgow, might possibly exaggerate or distort in reporting cases of which imperfect information alone could be obtained. To obviate this source of mischief, a book was opened at the sanitary office, in which the most strict directions were given that everything bearing on the possible advent of cholera was to be carefully entered and reported from day to day, even when the information obtained was open to doubt, the correction in this case being given after the investigation which immediately followed the report. This book was open to all the newspapers alike, and, in fact, to everyone anxious to be assured of the facts. By this means all merely sensational reporting was held in check, and a true statement of the facts each day was issued to the public. I am sure that a great deal of unnecessary excitement was obviated by this step.

In the course of August and September, 1866, the first cases of a suspicious kind were reported. In the middle of December all traces of an undue amount of diarrhœal disease had ceased. Before the first day of January, 1867, I was able to report the apprehension of epidemic cholera as having been entirely removed; and on New Year's day (always a popular holiday in Scotland) it became the duty of the medical officer to suggest (of course without any pretension to dictation) that the day might be fitly commemorated by a public service, or services, of thanksgiving to Almighty God, on the ground of deliverance from the threatened plague. The suggestion was largely adopted, many of the churches being opened on the occasion with a large attendance of devout worshippers, many or most of whom had intelligently followed the whole course of the proceedings here narrated.

On Good Friday of the same year (1867) a public meeting was

held in the City Hall of Glasgow, attended by a large number of the clergy and laity of various denominations, in which resolutions were passed commending the scheme of visitation by the churches during cholera to the notice of the public, as being fraught with almost indefinite possibilities of good, and as deserving of a more permanent existence. Several of the most eminent speakers—Drs. Norman Macleod, Marshall Lang, and others—enlarged upon the truly Christian character of the movement, expressing the wish that such a broad and practical Christianity as was evinced in this effort to remove the causes of disease might well be looked upon as alike a benefit to the population at large and to the churches themselves. The visitors employed on this occasion were almost unanimously of the opinion that both from the point of view of religion and of beneficence, it was highly desirable that such a movement of real Christian charity should be continued and perpetuated, if possible. The medical officer remarked on this occasion that an *auto da fé* (an act of faith) had at one time a very terrible and sinister meaning in the Spanish language, in the days of the Inquisition. Was it not within the compass of a more genuine and real Christianity, denuded of doctrinal distinctions, but tending ever to practical works of mercy and kindness, so to avail itself of movements of sanitary progress as to claim a share in them on the part of the church universal, undisturbed by sectarianisms, and in the name of the common Lord? Unfortunately, it was not possible so to apply in a permanent fashion the lessons of the cholera epidemic of 1866; but they remain, nevertheless, as a notable evidence of what may be done under the influence of like circumstances in future; and with this view I have now placed a brief sketch of the facts before this Congress.[1]

[1] A notable example of what Mr. Matthew Arnold might have called the "Philistine" point of view of these transactions was contained in the remark of a very eminent citizen of Glasgow at the time, viz., that after all the fuss made about the cholera, and all the expense incurred in its prevention, "*the cholera did not come!*"

APPENDIX.

Abstract of Instructions Issued from the Sanitary Department, Glasgow, 1866, in Respect to Asiatic Cholera.

I. "*Instructions for District Visitors in Time of Cholera or when Cholera is Threatened.*"

The object of these instructions was to place District Visitors in communication, on the one hand, with the people, and, on the other hand, with the sanitary authorities, with a view to the observation and reporting of removable defects; the procuring of external cleansing; the removal of night soil; the use of personal influence as to cleansing and ventilation; the opening of windows, or at least their construction so as to open at the top, in accordance with the law; the use of whitewash where necessary, the materials being furnished by the authorities on requisition of the Visitor; the use of personal urgency upon the inhabitants as to cleanliness of person, of clothing, and of bedding; and, further, all possible instructions concerning the use of plain, wholesome food, and of clean, fresh water and milk, with cautions against the undue use of strong drinks. It was further made part of the duty of the District Visitors to inform the inhabitants that "in all cases of diarrhœa, or of serious derangement of the stomach or bowels resembling cholera, persons should be recommended to go to bed, to keep quiet and warm, and to send instantly for medical advice."

II. "*Instructions for Medical House-to-house Visitors in Districts in which Cholera Prevails or Threatens to Prevail.*"

This set of instructions was much in accordance with the preceding, but was specialized by the medical character of the Visitor, and had general application to what is called "house-to-house visitation," so well understood and practised in former epidemics.

III. "*Instructions on Disinfection, for Medical Officers, District Visitors, and others, in Case of Cholera, Choleraic Diarrhœa, and other Diseases of Like Character.*"

This was a very detailed paper, involving all the principles of the germ-theory and of disinfection, as then understood, in reference to cholera—*e. g.*, indicating that "It has been ascertained by scientific investigation that cholera, although much less infectious or contagious (in the ordinary sense of the words) than such diseases as fever or smallpox, has the special property of communicating to the discharges from the bodies of the sick a dangerous quality; that these discharges may endanger life by soiling bed-linen, or vessels, or the floor, or the hands of attendants, or privies and water-closets, or collections of ordure in open courts, sinks, ash-pits, dung-steads, or common sewers, or, finally, by sinking into the ground, or otherwise polluting the drinking water; and that the danger is not diminished,

but rather (as there is reason to believe) increased, by decomposition of the choleraic discharges in connection with masses of ordinary filth. It follows, therefore, that all choleraic discharges, and all things soiled by them, should be disinfected and cleansed immediately; and where this cannot be perfectly done, the *dis*infection should be carried out in detail over the whole sphere of the *in*fection—*i. e.*, into courts, sinks, privies, ash-pits, dungsteads, common sewers, and in some cases into the soil and the water, as above described. It is further to be carefully kept in view, that these principles are to be applied not merely in cholera, but in every case which can be detected of diarrhœa or other disease carrying the suspicion or possibility of cholera; inasmuch as no practical security exists, on the great scale, for the freedom from infectious quality (in times when cholera is prevailing) of the discharges in any case of diarrhœal disease; and almost all cases of true cholera are preceded by a diarrhœa, which probably may endanger others nearly as much as the true cholera itself."

The methods of disinfection recommended were the adding to the suspected discharges, immediately, of a measured portion of the common green vitrol or sulphate of iron corresponding to a daily weighed quantity of about two avoirdupois ounces for an adult and one avoirdupois ounce for a child during each day in which the disease lasts, and, for at least several days afterward, until all possible risk is over; and, further, the disinfection of all matters capable of being so treated by the addition of carbolic acid in the proportion of a teaspoonful of ordinary commercial acid for the discharges of one individual for one day. In disinfecting clothing, chloride of zinc was recommended, and, speaking generally, the use of blue litmus paper, as regards all matter so disinfected, in order to secure a distinct acid reaction. Supplies of all these materials were kept constantly available, in a state for immediate use, and were to be had, on personal application, at the depots indicated by the authorities.

IV. "*Instructions for the Inspector of Cleansing, as to Disinfection in Cholera and Diarrhœa.*

This instruction need scarcely be given in detail. It was founded on the idea that the services of an inspector could be brought into immediate requisition, at any suspected point, both for the advice of the inhabitants and for practical work.

V. "*Instructions for Chemists and Druggists, and for all Persons Charged with the Supply of Disinfectants.*"

The supply was to be gratuitous, in divided quantities, which were carefully labelled and marked, "For one day's supply," and also with directions for use in accordance with the preceding. The depots at which these supplies were furnished were kept open day and night during the time when cholera was apprehended, and were so arranged that, throughout the whole city, a depot was available within a short distance.

VI. "*Plain Directions for the People. (For distribution by District Visitors.)*"

The object of this paper (covering four pages octavo) was "to represent to the people of the district what things are necessary to be done in view of an epidemic of cholora, and, if possible, so done as to prevent the epidemic from visiting Glasgow at all."

The inmate of the house is recommended to welcome the Visitor who delivers the paper, to talk freely with him, and to think carefully over what he says. The instructions given are under the following heads:

1. "Whoever would avoid cholera must, above all things, be clean; but cleanliness *out and out* is not always an easy matter. Think of these things for a little, viz.: Do you wash often and thoroughly and all over? Do you wash your children every day, and from head to foot? Do you keep no dirty clothes on your person or in the house? Do you allow no dirty dishes, no dirty plates nor spoons, no dirty towels, no dirty brushes, no dirty floors, walls, closets, beds, bed-curtains? Is the house always tidy and light and pure without and within? Do you always breathe a clean, pure air, by taking care to open the window very often? Do you use freely the great blessing of clean and pure water, as you may have it abundantly? or do you keep it in the house until it is tainted and unclean? Remember that unless you have clean air and clean water, there is no perfect cleanliness; and it is your own fault if you have not enough of both."

Paragraphs 2 and 3 contain similar details in regard to cleansing by the authorities, the use of unwholesome food, etc.

4. "Be equally careful of what you drink. All that has been said of eating applies also to drinking. And more: be sure that cholera will find out the drunkards first, and destroy them in the greatest numbers. It is a frightful delusion to suppose that you can keep away cholera by strong drink. Medical men of experience will tell you, with one accord, that tipplers have been by far the most numerous victims in all the epidemics."

5. "Ask your Visitor where to apply in case anything goes wrong. It is a mistake to suppose that cholera will strike you down all of a sudden: it will give warning, if you will take warning. Do not give way to alarm, therefore, but remember always that too much looseness of the bowels, especially if without a known cause and without pain, should lead you to give notice in the proper quarter, in order that a Medical Visitor may be sent with medicines and disinfectants, if you are unable to command them otherwise. There are few cases of cholera that may not be checked in the very earliest stages, and nothing, therefore, can be more unreasonable than to send for the doctor for the first time, in a hurry, after the disease has got beyond the power of medicine. It is quite true that very many cases of what is called diarrhœa have really nothing to do with cholera; but no harm is done by simply giving notice, and a little good advice at the beginning will save a great deal of trouble in the end—'a stitch in time saves nine.' These instructions are intended not to frighten you, but to lead you to be wise in time."

Enclosed in this paper, which was left in every household, was a slip corresponding with the section of the city in which the house was located, and giving at least names of three depots where every kind of written information or inquiry could be handed in, and where every kind of disinfectant recommended could be procured. A form for communicating such information as to the existence either of cholera or of simple diarrhœa in the house was supplied along with this paper, giving, *first*, the date; *second*, the patient's name and name of the householder where lodged; *third*, the age of the patient; *fourth*, a very exact definition of the address: the object being that the deposit of an information paper should be as promptly as possible followed up by a call either from an authorized and qualified medical practitioner or from one of the medical visitors employed by the authorities, and to whom it was confided to judge of the urgency of the circumstances with a view to further proceedings or to the administration of simple remedies.

VII. This last instruction, issued at the instance of the Secretary to the Privy Council, was for pilots, tug-masters, and masters of ships entering the Clyde, in reference to cholera and diarrhœal disease. It is noted as having been issued on the fourth day of May, 1866, and is signed by the Lord Provost of Glasgow and the Provost of Greenock; its object being to protect the ports by giving instant information of any case of suspicious disease, and offering hospital facilities for the treatment of such case. The instructions, however, proceed so directly on the basis of those framed in London and elsewhere, that it appears unnecessary to give them here in detail.

THE REMOTE RESULTS OF THE REMOVAL OF THE OVARIES AND TUBES.

By WILLIAM T. LUSK, M.D.,
PROFESSOR OF OBSTETRICS IN BELLEVUE HOSPITAL MEDICAL COLLEGE, NEW YORK.

It must be admitted in fairness, that the removal of diseased ovaries and tubes is followed in very many cases by the relief of local pain; that the removal of pus collections, whether in the tubes or ovaries, eliminates a source of danger to life; that, when properly performed, the dangers of the operation, *quoad vitam*, are small, not to be weighed for a moment against the terrors of chronic invalidism.

This statement purposely ignores the question as to how far in cases of tubal and ovarian disease laparotomy can be avoided, and equally good results be obtained by the healing influence of time and the procedures of minor gynecology, though incidentally I sometimes wonder whether the lofty contempt with which the minor gynecologist is regarded by the pelvic surgeon is fully warranted. At any rate there is another side to the story, as for instance: Not long ago a young woman called upon me with a tale of suffering, of months of treatment in a private sanitarium, and of her visit to a noted specialist, who assured her that castration alone could afford her relief; yet the replacement of a retroflexed uterus and the introduction of a pessary caused her pains to disappear, and at the end of a week she wrote that inasmuch as she was entirely well she had concluded to go home.

Now let us suppose that salpingo-oöphorectomy had been successfully performed in this patient's case, what would have been the subsequent history, *i. e.*, what is the usual later history of cases of double oöphorectomy, where the operation has been skilfully performed, and the recovery from the same has been speedy and complete. The central event is the cessation of the menses. This occurs, according to Glaevecke's[1] statistics, based upon those of Hegar, Wiedow, Tissier,

[1] Glaevecke: "Körperliche und gerstige Veränderungen im Weiblichem Körper nach Kunstlichen Verlüste der Ovarien," etc., Arch. f. Gynäk., vol. xxxv. p. 12.

Schmalfuss, and upon his own cases, in 86 per cent. either at once, or after a few recurrences of the monthly flow. Of the remaining 14 per cent., in some there is a marked diminution in the amount of the discharge, and in others the continuance is attributable to an incomplete removal of the ovarian tissue or to peripheral irritation from the ligated endings of the tubes, or finally to pathological conditions of the uterus or of the uterine mucous membrane.

In calling this the central event, I know I am treading upon the sensibilities of those who regard the castration of women as a matter of light importance. I acknowledge that it is to a great extent a figure of speech. I mean by it to indicate that the woman has lost in the disappearance of the menses the most distinctive sign of sexual activity. At the same time the uterus diminishes in size, the vagina becomes narrow and shrunken, and its transverse ridges are effaced. In many instances the vasomotor disturbances, such as the hot flushes and profuse perspirations, serve as efficient reminders that the climacteric due at fifty has been reached, let us say, at twenty-six.

It is customary to try and weaken the force of this conclusion by insisting that the removal of the ovaries does not impair the genital sense. Reliable statistics upon this point are not easily obtained. At least, so far as my experience goes, the subject is one which few women care to discuss. But enough evidence has been obtained to show that the sexual appetite is in some cases unimpaired, or it may even, for a time after the operation, be increased; that in others it is sensibly weakened, and in others again, it is abolished altogether. Zweifel's[1] statistics on this point are instructive. In reports obtained from twenty-six cases, no change was observed in ten patients; in three the desire was weakened; in three it was lost; while ten of the women reported they had never had any.

For those who regard the preservation of the sexual appetite as compensation for the loss of other feminine functions, it is well to bear in mind that, while it may be true, as has been maintained, that the sexual instinct is in man the most powerful incentive to exertion, in woman it is in the main subservient to the faculty of reproduction.

The young woman who has been deprived of her ovaries cannot marry without an explanation. If objection on the score of mutila-

[1] Zweifel: "Ueber Salpingo-oöphorectomie," Arch. f. Gynäk, vol. xxxix. p. 353.

tion is waived, and there follows a Malthusian union, it is certain that as life advances both husband and wife will have to struggle against the sadness and depression incident to a childless old age. The despairing cry of Rachel can possibly be better appreciated by an association of physicians than by the great pelvic surgeon, who, flushed with success, proudly vaunts his one hundred and something case, without a single death.

It may be said that all this is irrelevant; that the women from whom the tubes and ovaries are removed are already sterile. I have taken care, however, that that should not be the case with the young woman who has served as my text.

There is a question moreover whether there is not an unnecessary degree of fatalism in the assumption that inflamed and thickened tubes involve always permanent sterility. The reasoning in cases of operation is purely deductive, as the removal of the appendages puts an end to observation.

To me a certain amount of doubt has been suggested by the following occurrence in my practice. The patient, when I first saw her some years ago, was a young woman of seventeen. She had suffered agonizing pains at monthly intervals, and was confined to the bed or couch for the greater part of the time. An examination revealed occlusion of the lower vagina. An opening was made, and a large amount of retained blood and clots was removed from the upper vagina and uterus. The latter had been converted into a sac. For a long time thereafter the tubes remained thickened and tender. This was especially marked on the left side, to which the fundus of the uterus was drawn by peritoneal adhesions. Salpingotomy was plainly indicated, and I should have performed that operation had I obtained the patient's consent. Finally, however, she married. My advice in the matter was not asked. Last June the young woman called upon me. She had been married a year, and was seven months pregnant. The thing was inconceivable, but it was a fact.

So far it has been argued only that castration is followed by the symptoms and changes due to the climacteric. That this price may be joyfully paid by even young women to purchase relief from constant suffering, I readily admit. But when relief has been obtained, I have found very few intelligent women who under the shadow of the climacteric have not needed renewed assurances that the same end

could not have been obtained by more conservative measures. It is incumbent, therefore, on the operator to weigh this question carefully in advance, that he may not only give the required assurances, but that he may be able in so doing at the same time to retain his self-respect.

In my opinion most cases of tubal swelling yield to unheroic treatment. It is futile to claim that all will do so. For success patency of the tubal canal is necessary. Now, in a large number of cases where other means have failed, salpingotomy is capable of furnishing results that approximate to the marvellous. The enthusiasm of certain operators has this for a foundation. Because of the value of salpingotomy, its results should be subjected to the keenest scrutiny in order that its uncritical employment may not lead to its wholesale condemnation. This work cannot be accomplished by any individual. It must be the outgrowth of collective observation. Fortunately Mr. Tait has placed himself at the head of such a movement, and expresses his hope soon to publish an analysis of several hundred cases from his own unequalled practice. In a paper read during the present year before the Surgical Congress of Paris,[1] he admits the occasional occurrence of suppurating fistulous tracts, of fistulous communications with the bladder and intestines, of hemorrhages between the folds of the broad ligament, and that pelvic pains are not always relieved by the most carefully executed salpingotomy. This is wiser than the self-complacent attitude of some of his followers, who insist that all failures are the result of defective intelligence, or are due to lack of operative skill.

With the views I have expressed with regard to the curability of many forms of tubal disease, my own operative experience has been comparatively limited. Still, during the last five years, I find, in my records of abdominal sections, sixty-five cases where the uterine appendages were removed either for degenerative changes in the tubes or ovaries, or for the arrest of myomatous growths. I lost two of my patients. My statistics would have been better had it not been my misfortune to lose my sixty-fifth case.

After recovery from the operation a large number of the women treated have disappeared from sight; many have returned to express

[1] L. Tait: "Sur les Resultats Eloignés de l'Ablation des Annexes Uterines." Annales de Gynécologie, April, 1891.

their gratitude for restored health; a few, alas! still remain upon my hands, a source of perplexity and embarrassment. As months and years roll by, there gets to be a hollow ring to one's assurances that it is all right; that the benefits of the operation have only been delayed.

As an example of this, I beg to be permitted to relate the following history:

Mrs. X., æt. twenty-four. When I first saw her she was a chronic invalid. As she suffered from retroflexion, I first performed upon her Kelly's operation. The recovery was complicated by the formation of a sinus, which, however, healed after the expulsion of the silk ligatures employed in stitching the round ligaments to the peritoneal walls. Owing to persistent pains and profuse hemorrhages a year ago I removed the ovaries and tubes. Great care was taken to make the excision complete, as it was thought desirable to arrest menstruation. The tubes were thickened and contained a considerable quantity of muco-pus. The organs in the pelvis and the contiguous intestines were matted together by adhesions due to chronic inflammation. The patient showed little disturbance from the operation. Nevertheless there has been no cessation of the menstrual hemorrhage, and no improvement in her pelvic pains.

The reasons of failure or of retarded recovery have naturally been the subject of extended inquiry. For the most part, at least, the disappointing outcome appears to result from the incomplete removal of the appendages, from complications growing out of the operation, or because the morbid condition of the patient was not directly connected with the organs removed.

Hegar[1] enumerates as active factors in the causation of persistent pain, adhesion of the intestines to the stumps, irritation due to ligatures, and local inflammation of the peritoneal or of the pelvic connective tissue. These latter may be either the result of the operation, or they may be exacerbation of a previous latent inflammation.

In two of my cases the patients have returned because of abdominal hernias, and have required a special operation for that infirmity. The consequences of this condition are, according to Hegar, diminution of intra-abdominal pressure, with abdominal and pelvic hyperæmia involving the uterus likewise, meteorism of the intestines, and traction

[1] Hegar: Der Zusammenhang der Geschlechts Krankheiten mit Nervösen Leiden, etc. Stuttgart, 1885.

upon the suspensory ligaments of the chief abdominal viscera. If the opening is small, there is, in addition, a swelling of the protruded intestines, interference with the fœtal circulation, and reciprocal pressure between the intestines and the abdominal opening, with a multitude of associated nervous symptoms.

Mr. Tait reports four cases in which, because of the continuance of pelvic pains after operations, he reopened the abdomen. In three he found a cyst had formed near the amputated extremity of one, and in the fourth of both tubes. This secondary trouble he supposes had its origin in the uterine portion of the tube, the direction of the dilatation outward having been determined, probably, by the closure of the internal orifice.

In two cases of my own, in one of which two years, in the other five years, after removal of both tubes for pyosalpinx, I reopened the abdomen because of the patient's constant complainings. In neither was it possible to discover any hidden trouble. There were neither adhesions, nor thickenings of the tissues, nor cystic growth, nor disturbances caused by the ligatures. Though nothing was done except to explore, and then close the incision, both women brightened up for a time, and expressed a great sense of benefit from the operation—a benefit which, however, was of short duration. In these women it is more than likely that the intolerable pains complained of were hysterical in their nature. The term hysterical I use with reluctance, as one of the chiefest benefits derived from modern methods has been to remove from many women the stigma of hysteria, *i. e.*, it has been found in a large number of patients to whom the term "nervous" was formerly applied, and who were unceremoniously transferred from one hospital to another, the ailments are really dependent on reflex sources, and respond to intelligent treatment.

The favorable results in many cases of seeming mental and moral perversity relieved by the exsection of diseased uterine appendages has led to the trial of the operative removal of healthy pelvic organs for a variety of nervous derangements. As was to have been expected the result has proved a failure. In a few instances, contrary to my better judgment, I have operated in accordance with this indication, but I have never seen the slightest benefit accrue. The same wearisome experience has fallen to the lot of many of my colleagues. I am, therefore, tempted to assert that the performance of normal

ovariotomy for epilepsy and insanity is to be regarded as hardly better than malpractice.

The extent and frequency of serious mental changes as a consequence of the removal of the uterine appendages is another question which calls for very carful investigation. One of my patients, operated upon five years ago, is now insane. I know nothing of her family history, but can state that she was not "queer" at the time of the operation. The recovery from the latter was uncomplicated and she left the hospital "cured." There is no trace now of pelvic trouble, but the pains have returned, and she now sits all day brooding upon the change that has taken place as regards her physical state.

The reports of operations as to the connection of castration with mental changes differ widely. Some go so far as to deny any connection between the two events, while Glaevecke noted melancholia in eleven out of thirty-three patients of whose condition he was able to obtain accurate information. In the appended table, furnished me by Dr. C. C. Lee, which was compiled from carefully kept records, it will be seen that depression is noted in nine cases. In one instance at the end of a year, and in three at the end of two years, the patients recovered their wonted spirits. Two of the unimproved patients were epileptics. The experience of the neurologists, into whose hands this class eventually fall, is especially desired in regard to this question.

A review of the results of Mr. Tait's operation shows that, as a rule, the change of life is effected without unusual disturbances, without loss of womanly graces, and that the sexual appetite in many cases persists. On the other hand, in certain cases fistulæ, hernias, adhesions, local inflammations, aud a variety of psychical changes complicate the issue. In some instances the relief is immediate; in many it is long delayed; in a few it never comes at all.

Dr. Lee's report will be found most instructive, not only because of the care with which he followed up the later histories of his patients, but because the histories were derived from an exceptionally intelligent class. It does not tell a very encouraging story.

The more the question is studied, the more clear it becomes that the loss of her ovaries does make a difference to a woman. It is time to echo in this country Doléris's cry in France: "Too many useless mutilations; not enough conservative gynecology."

This is no discredit to Mr. Tait's operation. There will always be

a field for its beneficial employment, and its author never intended it as a panacea for every feminine ailment.

At the risk of having the finger of scorn pointed at me, I do not hesitate to confess that in cases of enlarged and tender tubes I resort to rest, the vaginal tampon, douches, massage, faradaism, and a tonic regimen. If the tubal swelling is intermittent, and is associated with a narrow cervical canal, I am not afraid to use Goodell's dilator to secure free drainage of the uterine cavity. If the damming up of secretions in the tubes is the result of adhesions, I try to break them up by combined manipulations, according to Schultze's method, provided the tube sacs do not contain pus. If I am in doubt as regards this point, I employ an exploring-needle passed upward through the vagina. I am in accord with Landau, Mundé, Grandin and others, who maintain that one can often effect a cure in hydrosalpinx by the withdrawal of the fluid through the vagina; and, in a pyosalpinx which is near the vagina, I do not hesitate to open and drain from below. If, owing to the presence of a pus tube, or of well-defined ovarian disease, or where, owing to uncertainty of diagnosis or failure of treatment, it is decided to open the abdomen, it will be well in future to consider the recommendations of Martin and of Polk, not in all cases to remove the entire organs, but to study in each case with care whether by removing simply the portion affected with disease it may not be possible at the same time to relieve pain and preserve the feminine functions.

It cannot be too often repeated that the successful removal of an organ is not a triumph of art, but a confession of defeat.

APPENDIX. This Table comprises only cases of abdominal section in which the uterine appendages were completely removed for causes other than tumor, and of which I have obtained frequent reports, so as to be sure of the after-condition of the patient until within the last six months. No laparotomies are included. About two-thirds were private patients, and one-third hospital cases. The latest was done five years ago.

September 8, 1891. CHARLES C. LEE, M.D.

Name, age, social state.	Date of operation.	Indications for operation.	Subsequent relief of local pain.	Secondary local effects of operation.	Effects on nervous system and on general health.	Effects on sexual appetite.	Resulting mental derangement.
1. L. V., 21, single,	April 26, 1883.	Dysmenorrhœa with epileptiform convulsions.	Partial for first year; after that complete.	Good in all respects.	Convulsions have disappeared; general health is good.	Unknown.	None of any kind.
2. C. J., 35, married, 3 children.	May 16, 1883.	Chronic ovaritis; dysmenorrhœa; constant pain.	Moderate for two years; since then quite good.	Quite good after first year, during which menstruation continued.	General health good; no neurotic symptoms; has become very fat.	Unknown.	None; spirits good.
3. H. C., 30, married, 5 children.	June 8, 1883.	Chronic peritonitis, with probable pyosalpinx.	Very trifling for two years; since then complete.	Generally beneficial. Some suffering from uterine prolapse.	General health slowly improved. No neurotic symptoms.	Unchanged; never very great.	None.
4. C. L., 24, single.	Oct. 6, 1883.	Constant ovarian pain with chronic ovaritis.	Complete.	None.	Generally good; patient well.	Unknown.	None; patient seems happy.
5. E.M.B., 30 married 6 years, sterile.	Jan. 14, 1884.	Dysmenorrhœa with prolapsed ovaries; nervous prostration	Very little for 18 months; since then considerable	Gradual but incomplete improvement.	Tardy improvement of neurotic symptoms and of general health.	Diminished.	None, excepting slight discouragement at slow improvement.
6. M.H., 28, single.	March 8, 1884.	Chronic ovaritis for 11 years; dysmenorrhœa; general asthenia.	Incomplete, but since second year considerable.	Menstruation continued for two yrs.; then stopped.	Very unsatisfactory; neurotic symptoms have continued.	Unknown.	Much mental depression at times, with insomnia.
7. E. M., 28, married, 3 children.	April 16, 1884.	Dysmenorrhœa; profuse menorrhagia; ovaries cystic; ill ten years.	Complete.	Pelvic peritonitis for two months; after that none.	Generally good; patient keeps well.	Unchanged.	None of any kind.
8. A. S., 37, single.	April 28, 1884.	Constant dragging pain in back; dysmenorrhœa; ovarian prolapse; ill ten years.	Partial for two years; recently much better.	Immediate cessation of menstruation.	Slight but steadily increasing improvement.	Unknown.	None of any kind.

Name, age, social state.	Date of operation.	Indications for operation.	Subsequent relief of local pain.	Secondary local effects of operation.	Effects on nervous system and on general health.	Effects on sexual appetite.	Resulting mental derangement.
9. B. B., 31, single, but has 2 children.	May 13, 1884.	Ill two years with salpingitis and intractable ovaritis.	Very marked, but with occasional relapses.	Menses ceased after two months; slight pelvic peritonitis.	Much improvement, but patient has become very fat.	Unchanged.	None; patient cheerful.
10. E.K., 20, single.	June 20, 1884.	Constant flooding; abdominal pain; ovaritis; ovarian prolapse.	Complete.	Slight pelvic peritonitis from rupture of a pyosalpinx.	Excellent in every way.	Unknown.	None of any kind.
11. C.W., 27, married, 3 children.	Sept. 24, 1884.	Pyosalpinx and ovaritis; intense dysmenorrhœa.	Entire.	Much hemorrhage from adhesions; drainage; pelvic peritonitis.	Very little for two years; since then constantly better.	Diminished.	Depressed for two years; since then cheerful and well
12. L. S., 25, single.	Oct. 5, 1884.	Cystic and prolapsed ovaries; dysmenorrhœa.	Partial only.	Perimetritis with increased uterine prolapse.	Unsatisfactory; one year later I had to do a hysterorrhaphy.	Unknown.	Much mental depression from failure of first operation to relieve.
13. I. A., 22, married, 1 child.	Nov. 19, 1884.	Chronic ovaritis; dysmenorrhœa; very hysterical.	Incomplete for one year; since then entire.	Menstruation ceased after four months.	Excellent after lapse of one year	Unchanged.	None of any kind.
14. M.B., 40, single.	Dec. 9, 1884.	Cystic and prolapsed ovaries; constant pain.	Incomplete because of resulting cystitis.	None; six months later a cystitis developed from cold and exposure only.	Marked improvement.	Unknown.	None, excepting hysterical depression during cystitis.
15. J. B., 30, single.	Jan. 10, 1885.	Pyosalpinx and adherent retroflexion of uterus; ten years ill.	Very gradual, but complete.	Improvement of all local conditions; operation with hysterorrhaphy.	No immediate effect; gradual benefit after one year.	Unknown.	None of any kind; patient generally well.
16. R.W., 23, single.	Mar. 18, 1885.	Cirrhotic ovaries; prolapsed with constant pain; intense dysmenorrhœa.	Imperfect; pain recurs still at intervals.	Menstruation ceased in four months. None other.	Slight improvement in both, but imperfect.	Unknown.	Much mental depression at times.
17. C. G., 26, married, 2 children.	May 16, 1885.	Ill 7 years; double pyosalpinx; dysmenorrhœa; constant pain.	Partial for six months; after that complete.	Menstruation ceased; slight perimetritis.	Decided and steady improvement in both.	Unaffected.	None of any kind.

Name, age, social state.	Date of operation.	Indications for operation.	Subsequent relief of local pain.	Secondary local effects of operation.	Effects on nervous system and on general health.	Effects on sexual appetite.	Resulting mental derangement.
18. M.B., 45, single.	June 16, 1885.	Ill 10 years; ovaries cystic and adherent; great pelvic pain.	Very slow and imperfect.	Secondary hemorrhage on second day; localized peritonitis.	Slight improvement after first year; never well.	Unknown.	Much discouragement; has since had electrical treatment without avail.
19. J. L., 30, married, 1 child.	Sept. 22, 1885.	Ill 3½ years; dysmenorrhœa; ovaries cystic and adherent	Partial for six months; after that complete.	Menstruation ceased at once.	Much cerebral fulness; "flushing" for one year.	Diminished.	Intensely nervous and hysterical for one year; since then well.
20. E. E., 26, married, 1 child.	Oct. 14, 1885.	Ill 3 years with ovaritis; intense dysmenorrhœa and pelvic pain.	Very slow, but complete in second year.	Secondary hemorrhage from apparent hemorrhagic diathesis; transfusion.	Extremely slow but complete recovery.	Unchanged; never much.	Much depression for first year; now quite bright.
21. C. H., 32, single.	Nov. 6, 1885.	Ill 6 years; chronic ovaritis; dysmenorrhœa; constant pain.	Complete after second month.	Menstruation lasted two months; slight local peritonitis.	Excellent in both.	Unknown.	None.
22. M. A. M., 31, married, 1 child.	Dec. 13, 1885.	Dysmenorrhœa; prolapsed ovaries; threatening insanity.	Pain intense for two or three months; then ceased.	Generally beneficial.	Great temporary derangement: gradual cure.	Unchanged.	Much depression for two years; now quite well.
23. E. S., 19, single.	Jan. 4, 1886.	Epileptic convulsions at menstrual period (only); chronic ovaritis for two years.	Slight for one year; after that complete.	None, except to force the menopause after second month.	No benefit of any kind; convulsions recurred as often.	Unknown.	Great depression at continuance of epilepsy; takes much bromide.
24. A. P., 31, married, 1 child.	March 2, 1886.	Ill 6 years; ovaritis; retroflexion of uterus; salpingitis.	Partial relief obtained very slowly; never complete.	Perimetritis; acute cystitis; vesical catarrh.	Operation inflicted serious shock on both; imperfect recovery.	Unknown.	Much depression for two years; spirits now good.
25. J. E., 23, single.	Mar. 18 1886.	Ill 6 years; epilepsy; dysmenorrhœa; ovaries cystic.	Complete after about six months.	Menses ceased at once; slight perimetritis.	Little or none; epileptic convulsions continue.	Unknown.	Considerable at times; derives a little help from bromides.
26. C. M., 40, married, 2 children.	May 13, 1886.	Ill 15 years; hæmato-salpinx; intense dysmenorrhœa, etc.	Gradual for three months; after that complete.	Menstruation ceased at third month.	Rapid benefit in both.	Unaffected.	None of any kind.

THE REMOTE RESULTS OF REMOVAL OF THE OVARIES AND TUBES.

By WHARTON SINKLER, M.D.,

PHYSICIAN TO THE INFIRMARY FOR NERVOUS DISEASES, PHILADELPHIA, AND NEUROLOGIST TO THE PHILADELPHIA HOSPITAL.

THE importance of inquiring into the remote effects of removal of the ovaries and tubes is apparent. Until within a short time but little has been written on this subject, but the interest of medical men is becoming excited, and we are beginning to find frequent communications regarding it in the medical journals and elsewhere. Of late years uterine and ovarian operations are becoming more and more common. Operators are multiplying, and as a result, operations increase in a geometrical proportion. To use the words of a writer in the *University Medical Magazine*:[1]

"The technique of oöphorectomy has been so thoroughly systematized, that in itself it is now one of the easier surgical operations. A first successful abdominal section seems to have the same effect upon an operator as the taste of blood upon the Indian tiger. A thirst insatiable is aroused, and life is spent in looking for new victims. Cases running into double and triple figures are cited, where all the worst features of the most stubborn nature have disappeared, as though the surgeon's knife were gifted with the power of an enchanter's wand."

Operators, as a rule, know but little of the condition of their patients after they have recovered from the immediate effects of the operation. They pass out of their hands and return to the care of the family physician, or if not relieved of the trouble for which they sought an operation, go to another gynecologist, or to the neurologist.

[1] June, 1890, p. 497.

A recent writer,[1] himself a laparotomist, says:

"Because of the fact that all of these patients are not under my care at present, it is not possible to give the exact percentage of those cured, improved, etc."

In considering the results of removal of the uterine appendages, two questions are to be considered. First, if the removal of the ovaries was resorted to for disease of these organs; and secondly, if the operation was done for the relief of disorders of the nervous system which were aggravated at the menstrual period, and which it was hoped could be cured by causing cessation of menstruation.

The referee has gone fully into the consideration of the results from a surgical standpoint, where the appendages have been removed for disease. I will only say that I have known many most satisfactory results to follow the removal of the ovaries and tubes for pyosalpingitis, ovaritis, and other inflammatory conditions of these organs, and the general testimony is, that it is in these conditions that the operation is followed by the best permanent results.

Through the kindness of many professional friends, a large amount of material has been placed at my disposal, and from this, from my own experience, and from the cases reported in the journals, I have drawn the conclusions that I now present.

The physiological effects appear to be the same, whether the organs removed have been diseased or healthy. The age at which the operation was done has some bearing on the symptoms which follow. Young subjects present more marked phenomena than older persons. When the uterine appendages have been removed before puberty, or near the beginning of the menstrual function, the development of sexual characteristics is arrested. If, however, these organs are removed after full womanhood, no change takes place in the peculiar feminine characteristics. These are universally admitted facts.

The phenomena which follow the removal of the ovaries, as Tait expresses it,[2] "match in all other respects the process of the climacteric change." This is about the gist of the matter. We find in

[1] Charles P. Noble, M.D.: Transactions of the Philadelphia County Medical Society, April, 1891.

[2] An address delivered to the French Surgical Congress at Paris, April, 1891. Medical Record, May 2, 1891.

almost all cases, as soon as the patient has recovered surgically, that the various symptoms belonging to the change of life are present. The most prominent of these are the flushings and sweatings so commonly seen at the menopause. These occur most frequently during the first few months after the operation, sometimes annoying the patient intensely.

Dr. Howard A. Kelly, of Baltimore, informs me that in his experience the flushes and sweats reach a climax in from three to six months, gradually disappearing by the time a year or a year and a half have elapsed. Women have told me that the flushings occurred as often as every few minutes during the entire day. This symptom begins to lessen at the end of a year, but may continue after three years have elapsed since the operation.

Disturbances of the heart's action are common, and rapid pulse—tachycardia—is a not infrequent symptom. Kisch[1] states that after castration in mature women, the operation is followed by atrophy of the internal genitalia, and attacks of tachycardia are frequent. The explanation depends upon the irritation of the nerve fibres included in the contracting and atrophying structures.

One patient, who was referred to me by Dr. Oliver P. Rex, presented the form of paræsthesia which I described some years ago, and which I then expressed the belief belonged chiefly to the menopause. The case is as follows:

Mrs. Y., aged forty-one years; married at nineteen years; has had six children, the youngest being fourteen years old. Menstruation regular until six months ago; there was cessation for seven weeks, and a hemorrhage began from the womb. An extra-uterine pregnancy was diagnosticated, and Dr. Parish operated three months ago, removing a three months' fœtus and both ovaries. The right ovary was diseased. The patient made a good recovery, and got up at the end of three weeks. Soon after this she began to have flushes of heat—has six or eight attacks a day. Five weeks ago began to have numbness in the right hand when she waked from sleep. At first there was numbness alone, then sense of prickling and pain, which would waken her from sleep. In a few days both hands were affected. Now both hands feel numb all the time—most intense in the fingers, and most markedly in the ulnar distribution. When she goes to sleep the whole arm becomes numb and painful, and she is wakened. "Sleep is out of the question," and she walks the floor most of the night. The color and temperature of the hands

[1] Wiener medizin. Presse, May 10, 1891.

is natural; sensation to touch and localization, and compass points, is normal, but she is awkward about sewing, buttoning her clothes, etc. Dynamometer: R. 60, L. 40. Three years ago the patient had an attack of numbness in the hands after a night's sleep and after washing. This got well in a month.

The patient is more nervous since the operation, but only three months have passed, so this is hardly a fair test. She never had much sexual appetite, and has still less since the operation. I may mention that the numbness was relieved by full doses of ergot.

There is a widespread impression that women upon whom this operation has been done gain in flesh rapidly and become coarse and masculine in appearance. This is entirely erroneous. When diseased and suppurating ovaries and tubes are removed, the patient is generally in a condition of extreme emaciation at the time of the operation, and after recovery speedily becomes fleshy—but she rarely becomes stouter than she had been before when in good health. Occasionally a woman is seen whose ovaries have been removed for some disease of the nervous system, who becomes stouter than ever before in her life; but it has never been my experience to see or hear of one who has become unfeminine in the contour of the bust or limbs. The alleged growth of coarse hair on the lip and chin is unusual, and does not occur any more frequently than it does in women whose ovaries have never been tampered with.

Patients often suffer from various nervous troubles after removal of the uterine appendages; they may be restless and irritable or depressed mentally. This seems in many instances to be due to cerebral hyperæmia. The extent of mental disturbance varies in degree and duration. In some cases there is merely mental depression or mild melancholia, but in others there is either acute mania immediately following the operation, or a mild form of insanity gradually deepens and becomes a chronic mania. Coe[1] declares that there frequently follow this operation, persistent cerebral hyperæmia, ovarian psychoses, and even active insanity. Glaevecke[2] insists that in nearly all cases where the ovaries were removed the mental condition was decidedly affected, in many instances a condition of melancholia being produced. This statement is undoubtedly too extreme, but the number of cases of insanity following oöphorectomy is large.

[1] Medical Record, April, 19, 1890.
[2] Arch. f. Gyn., Bd. xxxv. H. 1.

In connection with the cases of acute mania which follow immediately after removal of the ovaries, it is only fair to call attention to the fact that acute mania may follow other surgical operations. I know of two cases, one a patient of my own, in whom an operation upon the spine was followed by active mania. Recently Dr. Simes[1] has put on record a case of insanity following oöphorectomy:

The patient had suffered from dysmenorrhœa and uterine hemorrhage, and both ovaries and tubes were removed. The ovaries were found to be normal but the tubes were enlarged to three or four times the natural size. On the fourth day after the operation the patient showed evidences of mental disturbance, and in a short time became actively insane. In six weeks she had to be removed to an asylum, where she remained for two months, and was discharged well. Several months later she thought her mind was not as good as prior to the operation. Her memory was bad and she could not think as well as she used to do. She was melancholy, and had a tendency to fall asleep during the day. Four months after the operation she menstruated, three months later there was a free uterine hemorrhage, and two months after another slight hemorrhage. She had still occasional sharp uterine pain.

Tait[2] admits that several of his patients "became queer for a short time—that is, they were eccentric and ill-tempered." Later in his address he says that he knows of no case of insanity in his practice.

Dr. C. T. Dent[3] thinks that insanity as a sequela to surgical operation is less uncommon than is usually supposed. He thinks that the mental impression may be produced in three ways: by anticipation, by actual operation, and by after-effects. The grades of mental disturbance following operations which he mentions, are: emotional disturbance, hysterical disturbance, loss of control, unreasonableness, hallucinations, and mania in its various forms. He refers to a paper by Savage, late superintendent of the Bethlehem Royal Asylum for Lunatics, London, upon "Insanity Following Anæsthetics."

Dr. T. Gaillard Thomas[4] has recently read an important paper before the New York Academy of Medicine, upon "Acute Mania, Melancholia, and Hypochondriasis as Sequelæ to Gynecological Oper-

[1] Medical News, June 20, 1891.
[2] Medical Record, May 2, 1891.
[3] Journal of Mental Science, April, 1889.
[4] Medical Record, April 20, 1889.

ations," which evoked considerable discussion at the time and afterward, in which reports of numerous other cases have been presented. Thomas reported six cases—of these six cases, two were abdominal sections, two were removal of the breasts, one operation for lacerated perineum, and one for lacerated cervix. He remarked that the entire number of cases reported, including his own, amounted only to twenty-six. He suggested the following questions: Are the cases of mania and melancholia due to the operation which antedated them, or do they follow as mere coexisting states? Secondly, any great mental strain might be followed by mania, and was it remarkable that, out of the large number of gynecological operations performed in the last quarter of a century, that this number of cases of insanity should occur? Were the operations in gynecology more likely to disturb the condition of the mind than other surgical operations?

Dr. Polk thinks that women are more disposed to maniacal disturbance after operations, especially gynecological, because, in his opinion, women are more emotional.

Mairet, of Montpellier, has collected twenty-five cases of insanity following operations from his personal experience, from which he draws the following conclusions: That individuals who are predisposed by heredity or other causes are prone to insanity after surgical operations; that the anæsthetic and the degree of surgical traumatism produce the most marked effects upon the brain.

Dr. William Goodell, in a personal communication, states that "two of his patients who were not threatened with insanity previously became insane a few months after the operation; and one young lady, from whom he removed two large ovarian cysts, had, after the lapse of six months, an attack of acute mania from which she died in a few days."

Dr. Graeme M. Hammond has sent me the notes of a case in which acute insanity followed the operation of ovariotomy in four or five days. The patient had previously shown no evidence of mental disease. At first there was violent mania, which abated in a few days, and a condition of chronic dementia took its place.

Dr. E. E. Montgomery, who has kindly sent me notes of between twenty-five and thirty cases, in which he had removed the ovaries two to three years ago, records two who became insane after the operation. In one of these there had been previous attacks of insanity,

and in the other hystero-epilepsy had been a conspicuous feature previous to the operation.

I have had under my own observation several cases of insanity after removal of the ovaries. The mental disturbance came on several months after the operation, and gradually deepened into insanity. While I do not believe that, as has been asserted, insanity follows in ten per cent. of the cases of hysterectomy, still there are a large number of cases in which some form or other of mental disease does occur as a sequela of the operation. In many cases there is merely some peculiarity or idiosyncrasy which is overlooked, or considered a passing condition, but too many cases of grave insanity have been reported for us not to consider very seriously the risk of mental effects when the operation is performed.

The consensus of opinion respecting the sexual appetite after castration in women, is that it is but little affected. Prof. Goodell, in the communication referred to above, states that his experience is that immediately after the operation the sexual desire is not lessened—in fact, it may be increased, but after the lapse of two or three years it decreases, and becomes finally lost. Dr. Howard A. Kelly expresses the opinion that the sexual appetite is unchanged by castration. Of fifty cases which I have examined, either personally or from notes sent to me by medical friends, I have found twenty-three in which information in regard to this question could be obtained. In fourteen of these it was asserted that the sexual appetite was the same as before the operation, and that the act was performed normally. In several the act seemed to cause pain after two or three years had elapsed since castration. In five cases the appetite had lessened. In two there was no sexual appetite, and the patients declared that it had never existed. In two the appetite increased after the operation. In a case communicated to me by Professor Keen, the sexual desire was excessive for two years after castration, but after this time it has become about normal. In considering the effects of the operation upon the sexual appetite, one must take into consideration the large number of women who are naturally without any sexual feeling.

The effects of the removal of the ovaries upon sexual appetite proves what has been long believed to be the case, namely, that the sexual desire does not depend upon the ovaries, but upon the centres in the spinal cord. Cases of onanism have been unaffected by removal

of the clitoris, labia, and ovaries. I have seen two cases in which onanism persisted after the operation to the same extent as before.

At the Berlin International Medical Congress, in 1890, Dr. F. Deppler, of Venice, read a paper embodying the results of a study he had made in the cases of ovariotomy performed by himself. He had performed castration forty-six times, obtaining a cure in thirty-nine cases. The operations were for purulent or gonorrhœal salpingitis, oöphoritis, fibroids of the uterus, etc. The following are some of his conclusions, derived from a study of the physiological consequences of the operation:

The breasts grow smaller, acquiring a strong resemblance to the male mammæ. The brown pigmentation of the nipple areola, perineum, and anus disappear wholly, as do also pathological pigmentation existing in some of the cases; the hair also turns white. The tendency to *embonpoint*, which is generally believed to exist after these operations, was not observed by the author. No changes were observed as regards growth of hair or the tone of the voice. The sexual desire remained, and was more pronounced the earlier in life the operation was performed. The operation offers no impediment to marriage; three of the author's cases had married and lived happily with their husbands for many years. In cases operated upon for uterine fibroids, the patients, even those in full maturity, lose all sexual inclination after the operation. In cases operated upon in early life for inflammatory conditions, no neuroses were seen to develop, which was not the case where women were operated upon late in life for fibroid tumors of the uterus.—*Medical and Surgical Reporter*, May 9, 1891.

As to the benefit derived by patients who have undergone oöphorectomy for insanity, epilepsy, hysteria, and the different forms of neuralgia and nerve troubles, the opinions of different observers vary to such an extent that we might believe that totally different beings and conditions were considered. Certain writers give the most glowing accounts of the benefit obtained by almost every patient operated upon, while others regard the results as being always so unfavorable that the operation is never justifiable. For instance, Dr. Ross, of Toronto, says that the removal of the appendages is never a legitimate procedure in a case of purely functional neurosis, and that even when marked structural disease of the appendages coexist, with severe neurotic conditions, the latter should be treated in the first instance in the hope that operation might be avoided.

A recent writer,[1] replying to the argument of Dr. Yarnal (*Medical Index*, April, 1891) against what he terms indiscriminate operations on the sexual organs, says: "If palliative treatment does give temporary relief to many, why waste valuable time?" and goes on to give many reasons for urging immediate operation.

"Though the 'leaven' of McDowell," she declares, "has not yet been potent enough for the whole medical mass, yet it has acted upon some portion of the lay mass; a woman now and again rises and asks for an operation. By so doing she shows fortitude and judgment that is beyond the comprehension of physicians, who look only at the mortality of operations upon cases *in extremis* from delay. Certainly the woman is right rational, not crazed, when she takes measures that will bring relief or death; that will make her generally useful, as against being made use of by the one member of society, to wit: the pseudo-gynecologist, as a filler of his purse."

As is generally the case, the truth lies between the two extremes. There certainly are a large number of cases of hysteria, neurasthenia, and allied conditions, depending upon diseased ovaries, which do not get well under the most judiciously applied treatment, and who do make a good recovery after the removal of the offending organs. In cases of extreme dysmenorrhœa this is conspicuously true. A patient suffering from the more severe forms of pain at the menstrual period barely recovers from one period before another comes. On the other hand, a vast number of patients have had their ovaries removed for hysteria, insanity, and the like, who are temporarily relieved by the operation, but in a few months were in as bad a condition as ever, and who recover permanently after a course of systematic treatment directed to the nervous system.

Dr. Weir Mitchell has communicated to me several cases which have been under his care which had been condemned to lose their ovaries, and who nevertheless grew strong and well after a course of rest treatment. One of these was a lady who was seen by three of the most prominent gynecologists in this country, and decided by them to have the only prospect of recovery in removal of the ovaries. She became entirely well without operation.

At a meeting of the Obstetrical Society of London, January 7, 1891, Dr. Playfair read a paper on "The Removal of the Appen-

[1] "Too Much Conservatism," by M. Fisher, M.D, Kansas City Medical Index, July, 1891.

dages of the Uterus for Neuroses." (*British Medical Journal*, Jan. 17, 1891.) He detailed several cases that had come under his observation: First, a case of neurosis treated by the removal of the appendages without benefit, subsequently cured by systematic treatment; and a similar case in which the operation was recommended and about to be performed, when the patient refused her consent—likewise cured by systematic treatment; third, a case of neurosis in which there was distinct evidence of structural diseases of the appendages. In this instance the neurotic symptoms were first dealt with in the hope that the patient would be sufficiently bettered to avoid the necessity of operation. The subject of hystero-epilepsy and mania, treated by removal of the uterine appendages, was considered. The general conclusions arrived at were: That the removal of the appendages is not a legitimate procedure in case of purely functional neurosis. Second, that when marked structural diseases of the appendages coexist with severe neurotic conditions, the latter should be treated in the first instance, in hope that operation might be avoided. Third, that in hystero-epilepsy and hystero-mania the results of operation have been so unsatisfactory that it is a procedure of very doubtful expediency, and not to be recommended.

In the discussion which followed Sir Spencer Wells quoted from a paper of Dr. Ross, of Toronto, who says that, in his opinion, to operate on organs not diseased, for the relief of undefinable symptoms, hysterical symptoms, or epileptic symptoms, is unwarranted.

"I have seen," says Dr. Ross, "these unjustifiable operations done both in Europe and America. Many cases in which ovaries and tubes are removed to relieve certain nervous symptoms remain unrelieved. Many cases I hear of as cures are not cured. From our failures to remove nervous diseases, as hysteria and epilepsy, by castration, we can see that the ovaries play but a part in their causation, and I believe that we might as well hope for relief of those diseases by enucleation of both eyes, as by removal of both ovaries, or both tubes, or both tubes and ovaries, or even tubes, ovaries and uterus."

He related a case in which he had removed the ovaries in 1886. In 1888 he was able to report that his patient had been in splendid health ever since operation, but in 1890 he had to say: "Her mental condition is not what it was before; she seems lazy, indolent and fat, and is not the bright little woman she was before the operation, even when she had her aches and pains." He also referred to a case in

which a woman of his acquaintance was operated on, and her case was brought before the Gynecological Society in December, 1888, very soon after the operation, as a practical cure. Sir Spencer Wells stated that he had seen the lady that day. She had never been well since the operation, but very much worse than before, and her case, instead of being a cure, was a deplorable and disastrous failure. He had seen other cases almost as unsatisfactory, and he fully concurred in all that Dr. Playfair and Dr. Ross had said against unnecessary and unjustifiable mutilation for transitory disease.

Dr. Alex. J. C. Skene, although himself a gynecologist of large operative experience, opposes the removal of the ovaries and tubes for chronic ovaritis.[1]

"It is true," he says, "that chronic ovaritis does not end fatally, and is self-limited, though often of long duration. The removal of the ovaries is not free from all danger, though all cases properly operated upon have recovered, and the operation may not in all cases give complete relief. In fact, many of the cases are not much, if at all, improved; even those who are nearing the menopause, and who bear the loss of the ovaries better than younger subjects, occasionally suffer much from those nervous disturbances which follow an abrupt menopause, and have to endure pelvic pain in the region of the stumps. The clinical history of cases in which the ovaries have been removed does not, in all cases, show great advantage over those in which the ovaries are left to complete the natural history of the disease. Younger subjects do not bear the loss of their ovaries agreeably. Some become fat, indolent, inefficient and subject to headache; others are irritable, dyspeptic and despondent, while but few enjoy general good health and mental vigor. This statement is contrary to much of the published literature, but is closer to the actual facts."

Brodwitz,[2] in a paper on the ultimate results of castration, concludes that

"In cases of general neurosis (hystero-epilepsy and epilepsy) the ovaries simply share in the central trouble, and hence castration cannot be expected to give relief. The ordinary sequelæ of castration are molimina, congestions, cardiac disturbances, flushings and vertigo, together with diminished sexual feeling in about two-thirds of the cases. Melancholy and forgetfulness are quite common, which may culminate in more pronounced psychoses."

At the fifth French Congress of Surgery, held in Paris from March 31 to April 4, 1891, one of the questions for discussion was, "What

[1] The Medical News, June 13, 1891.

[2] Inaugural dissert, Strassburg, 1890. Centralblatt für Gynäkol., 1891, and Amer. Journ. Med. Sci., June, 1891.

are the after-results of the extirpation of the uterine appendages in the non-neoplasmic affections of these organs?"

Sir Spencer Wells opened the discussion by saying that he continued to be favorable to the operation, but still he thought that it was too easily resorted to. Mr. Lawson Tait repudiated the statement that permanent evil results followed removal of the tubes and ovaries for disease of the uterus or its appendages, or for the relief of nervous disorders. He maintained that the changes immediate and remote which followed the operation were analogous to those which take place at the menopause. He thought it a wrong statement that 10 per cent. of the castrations for uterine fibroids bring on insanity. He thinks that in castration for nervous disorders he has not operated early enough, and he also thinks that in these cases we should operate more often than is now done.

In the same discussion a number of speakers gave their experience as to the late results of removal of the appendages. The majority seem to have considered that the results after removal of diseased organs were generally favorable, but when for nervous diseases the after-results were unsatisfactory. For example, Dr. Jacobs, of Brussels, had operated upon 58 patients since 1888; his conclusions were that the distant results are favorable in cases of suppuration of the appendages, less so in catarrhal affections, while in nervous women castration is rarely of any benefit.

Professor Le Dentu, of Paris, had operated 34 times. He thought that the after effects varied in different cases. Nervous patients, he thought, suffered much longer than others. He called attention to a peculiar after-effect in the case of a woman operated upon in 1888 In 1890 she returned suffering from violent pain in the left side, extending to the face. A small tumor was found in the vaginal cul-de-sac. Uterine dilatation was performed. On the twelfth day a large quantity of black liquid was evacuated. Since then the tumor and pain have disappeared.

Professor Bouilly, of Paris, said that the after-effects are favorable when one has to deal with salpingitis, but such is not the case with interstitial catarrhal salpingitis. As to interference with nervous phenomena he does not advise it.

Dr. Routier, of Paris, had since 1887 removed the appendages 52 times. The results were excellent in the great majority of these cases,

that is, in pyosalpingitis the results were generally good, but in certain young people the suppression of menstruation is followed by a "state of uncertain health."

Dr. Doyen, of Rheims, had done 32 laparotomies, in which 3 had died from the operation; in 3 the results were negative, 1 suffering from double purulent salpingitis, and the other 2 being extreme cases of hysteria. Seven continued to suffer with abdominal dragging-down pains, neuralgia and gastric crises. In 20 the results were satisfactory.

The immediate result of removal of the ovaries is almost always relief of the symptoms for which the operation was done. It is probable that in many of these cases almost any surgical operation would have been followed by the same relief. After a few weeks or months the old symptoms are likely to recur. I may be permitted to relate the case of a patient who came under my care after removal of the ovaries by one of the most distinguished laparotomists of this country, who has been identified with the operation of oöphorectomy since its inception. The following history was sent me by the family physician:

Miss A. was a puny delicate child from birth up to six years of age, but from that time until twelve she enjoyed good health. At that time she went to a boarding-school, and during the first year her health became so seriously impaired from dyspepsia that she had to leave school. Change of climate restored her to health; but two years later, on returning to her home in a malarious climate, she lapsed into a dyspeptic condition, and has been a sufferer ever since. In the spring of 1888, when twenty-one years of age, she went to a mountainous region with the hope of improvement in her general health, but soon after getting there she began to have violent nervous attacks attended with convulsions, which lasted many hours. These attacks were repeated at shorter and shorter intervals until they came daily. The affection was considered to be due to the womb or some of its appendages, and in August, 1888, the patient was taken to Dr. Battey, who removed both ovaries. She made a good recovery, and improved in her general condition very much, having no more convulsions until November, 1888, when she had one, and was then free from them for a year.

About two months later she took cold, and upon her arrival at home had several severe paroxysms of dyspnœa. The dyspepsia returned in a short time and soon became so much worse that but little, if anything, in the way of nourishment could be retained. Rectal alimentation had to be resorted to. In November, 1889, she had another convulsion, and this was followed by several others. "The convulvions come on with very brief intimation of

their approach—they are generally preceded by more than the usual amount of nausea. She will say that she feels dreadfully nervous, and in a few minutes becomes rigid and the convulsions follow. There is serious danger of her injuring herself in her tossings if not restrained. In some of her attacks it has required three or four persons to hold her on the bed. She bites herself during the attack. Chloroform, hypodermic injections of morphia, and everything else that has been tried seem to aggravate instead of relieving. There had been no irregularity of menstruation prior to the operation of oöphorectomy and no dysmenorrhœa."

In conclusion, the doctor urged upon me very strongly the fact that the patient could not take milk under any condition. "She has tried it fairly, and is always made severely sick by it." She came to Philadelphia in December, 1889, when I found a sallow and much-emaciated woman, who was very weak and very nervous. She vomited within a short time after taking food of any kind. I placed her in a private room at the Infirmary for Nervous Diseases, and told the nurse in charge of her that if she had a convulsion she was to be allowed to roll on to the floor from the bed without hurting herself, and to be left alone until the convulsion was over. She had but one after admission. In spite of the warning against milk, she was ordered small quantities of peptonized milk, repeated at short intervals. This was retained and the quantity gradually increased. To make a long story short, I will merely say that she was given a thorough course of the rest treatment, including massage and electricity, and moral influences were very strongly enforced. In a little less than four months she had gained thirty-five pounds—from ninety to one hundred and twenty-five pounds. She was able to eat any kind of food without discomfort, walked two or three miles at a time, and, in short, was a useful member of society. I have recently heard of her as being perfectly well and strong notwithstanding the fact that she has been living in a trying climate and having many arduous duties to perform.

I could add many similar cases, and so can every physician who sees much of nervous diseases.

Cases of insanity which occur only at the menstrual period, and cases of erotomania are often relieved by castration, and a number of permanent cures have been reported.

Goodell[1] says: "Insanity, when limited to the time of the monthly periods, shows an ovarian origin, and the removal of the ovaries will then very generally cure the mental disease. . . . But, on the other hand, if the insanity is constant, though exacerbated at the monthly periods, the removal of the ovaries does but little good. . . . Another important fact that I have learned by experience is, that the removal of the ovaries cannot be depended upon for the immediate cure of nymphomania or of other erotic forms of insanity."

[1] Medical News, May 17, 1890.

Tait, in the address referred to above, speaks of three cases of insanity which have been cured by removal of uterine myomata. Dr. Mitchell has related to me a case of insanity with erotomania in one of his patients, which was cured by castration. Prof. Keen, who has been kind enough to send me notes of ten cases in which oöphorectomy was done by him, gives the histories of two cases of menstrual insanity which were completely cured by the removal of the appendages. One was well after five and the other after ten years.

Prof. Goodell, in the communication already quoted, gives twelve cases in which oöphorectomy was done for insanity or mental depression. The results were:

Mental depression, cured	1
Insanity, cured	5
Insanity, improved	2
Insanity, not cured	3
Insanity, made worse	1

A number more of instances of cure of insanity by removal of the ovaries could be quoted, but the above are illustrative of the experience of prominent surgeons. On the other hand, a number of cases can be detailed in which the insanity for which the operation was done was either not relieved at all, or the "cure" was only temporary.

Professor Keen has related to me one case in which the ovaries were removed for dysmenorrhœa, and an unbalanced condition of the mind ensued. There was temporary benefit, but later the patient became insane. I recall a patient in the insane wards of the Philadelphia Hospital, whose ovaries were removed several years ago in the hope of curing hysterical insanity. She was temporarily benefited, but relapsed into a condition of mania, and had to be placed in the asylum.

The result of many operations for insanity indicates that a number are cured, but that most of the cases are those which were due to dysmenorrhœa, or were associated with the menstrual periods. When connected with erotic ideas, or masturbation, they are seldom benefited. If there is no periodicity in the insanity, and no evidences of dysmenorrhœa, or sexual disturbance, removal of the ovaries rarely does more than temporary good.

Prof. Goodell[1] says:

"In one of my cases, excessive masturbation was not only kept up after the operation, but it was actually enhanced by it for at least a year, when the habit

[1] Op. cit.

was finally overcome. In another case, the erotic impulses lasted for over a year; but they ultimately ceased, with the complete loss of the sexual feeling."

I have written to the physicians in charge of the largest asylums for the insane in Pennsylvania, asking if they had among their patients any in whom the ovaries had been removed. Had time permitted, I might have made inquiries of a larger number of institutions, still the replies which I have received may be fairly considered as a sample of what would be had from others. Moreover, it might be said that the inquiry was one-sided, as it would not show the cases in which the operation had been successful.

Dr. Chapin, of the Pennsylvania Hospital for the Insane, writes:

"In reply to yours of the 13th, I will state that since September, 1884, the date of my connection with this hospital, two women have been received whose ovaries had been removed for disordered mental condition. I do not think the operation was followed by improvement in either case, and one was certainly not as well, having delusions about the operation and her changed sexual condition. I have seen one patient outside the hospital whose ovaries had been removed, and the insanity continued."

Dr. John C. Hall, Superintendent of the Friends' Asylum for the Insane, Philadelphia, writes:

"I have seen several cases where the operation has been performed, and in only one has it produced any benefit. This lady is a case of recurrent mania, and I look for her to come back sooner or later. To my mind, such operations performed after mental symptoms have developed are not productive of good results, unless in such rare cases where the ovaries are very much diseased, when only partial relief could be expected."

Dr. Amelia Gilmore, resident physician in the woman's department of the Philadelphia Hospital for the Insane, writes:

"Yours, in relation to removal of the ovaries for insanity, is received. Besides Clara G. [the case to whom I have referred above], I have at present two patients who have had the uterine appendages removed, Maggie D., an epileptic, and Annie McG., who has recurrent attacks, with an alcoholic tendency."

Dr. S. S. Schultz, of the State Hospital for the Insane at Danville, Pa., states that he has had no patients on whom the operation referred to has been done.

Dr. Alice Bennett, resident physician of the department for women in the State Hospital for the Insane, Norristown, Pa., says:

"So far as I can recall, there are two cases now in the hospital in which the ovaries were removed for insanity.

Dr. A. H. Hutchinson, Superintendent of the Western Pennsylvania Hospital for the Insane, writes:

"During my entire residence of thirteen years in this institution I have known of but three cases who have been operated upon. Two were old cases of insanity, and the operation was performed three years ago; one is still a resident of this institution, has been insane several years, and is very crazy yet. The other patient was discharged from here improved, but two years after the operation suffered another attack, and was sent to another hospital, and is improving, but still is not well mentally, though able to be at home. The third case was operated upon just recently, and is one of acute melancholia. She is still a patient with us, and I think will recover after a while, though her recovery will not be permanent. She recovered in this hospital from her first attack two years ago. My experience is limited, as you will see, but I am not very much impressed with its importance, and have never recommended it. The operation has always been done by some outside physician, and at the request of friends."

The late results of castration in cases of epilepsy and hystero-epilepsy are even more unsatisfactory than in insanity. There is almost always temporary relief, just as is the case after trephining, but there is a recurrence of the attacks within a few weeks or months. Dr. Graeme Hammond has communicated to me a case in which epilepsy came on almost immediately after an operation for removal of the ovaries. Goodell gives one case of epilepsy cured, one "improved," and two not improved by removal of the ovaries.

Dr. Engelmann, of St. Louis, has communicated to me a most interesting case of an idiot girl of nineteen years, who had never menstruated. She was also epileptic. The attacks came on just before the time when menstruation should have begun; and they continued to occur at monthly periods—so an operation seemed to offer a prospect of success. The ovaries were removed at the urgent request of the parents. The patient improved greatly after recovery from the operation. She was reported to have no fits for two years, became much more intelligent, and in fact was stated by her family to have become a useful member of the household. Had the history of the case ended here, it would have been worthy of being placed among the great achievements of the gynecologist; but I have received a later account of the case, through the kindness of

Dr. W. B. Dorsett, of the Female Hospital of the City of St. Louis, under whose care the case had been. He states that the patient died May 3, 1891, in a convulsion. Dr. Dorsett thinks that the improvement which followed after the operation might have been due to hypnotic suggestion, as he practised it upon her daily for six months while she remained in the hospital. After the patient returned home her parents represented her as being better than she really was.

Dr. Engelmann also related to me two other cases of epilepsy in which the appendages were removed. In one there was improvement but not complete relief. In the other there had been a gradual disappearance of the attacks. In one of Dr. Price's cases there was complete relief to severe attacks of hystero-epilepsy after oöphorectomy, although after an interval of a year she had another attack after taking ether for the removal of an ingrowing toe-nail.

A patient under my own care had most violent attacks of hystero-epilepsy after removal of the ovaries.

The trouble is to determine whether the cases which have been apparently cured by castration have really been cases of true epilepsy or were only cases of hysteria.

When the operation has been done for the relief of pelvic pain it does not by any means invariably accomplish its object. If the pain is due to inflamed or diseased conditions of the structures, the pain is often relieved for the time, but before many months returns in the stumps of the ovaries, to be more severe than ever. When the pain is neurasthenic and not associated with disease of the ovaries, removal of these bodies seldom gives relief.

To sum up:

The remote effects of removal of the ovaries and tubes upon the general health is, as a rule, to improve nutrition and to better the strength, especially if the operation has been done for diseased ovaries or pus tubes.

That excessive gain of flesh is rare, and that change of voice, growth of hair upon the face, and loss of feminine characteristics do not occur.

That the sexual appetite in women is seldom changed by castration within two or three years after the operation, but after several years it becomes lessened.

That it is often the case that after this operation patients are more

nervous than formerly, and mental disturbances of various forms, insanity and epilepsy, not infrequently follow it.

That the influence of the operation is sometimes good upon insanity and epilepsy which are associated with severe dysmenorrhœa or occur periodically at the menstrual epochs; but when the insanity is constant, although it may be aggravated at the monthly periods, removal of the appendages is of no benefit. Hystero-epilepsy is seldom permanently cured by the operation. Prolonged after-treatment is generally necessary to relieve such cases.

Local pain is often not relieved by the operation.

Certain cases of neurasthenia which are associated with dysmenorrhœa, or with structural changes of the ovaries, are cured by the operation; nevertheless, no such case should be subjected to the operation without beforehand having the benefit of prolonged and patient treatment. It is unjustifiable to remove the ovaries and tubes in cases of neurasthenia, hysteria, etc., when these organs are healthy.

Many prominent gynecologists, including Goodell, Kelly, Price, and others, say that now they seldom remove the appendages for nervous diseases if the organs are sound and healthy.

ON THE REMOTE RESULTS OF THE REMOVAL OF THE OVARIES AND TUBES.

By JAMES J. PUTNAM, M.D.,
INSTRUCTOR IN DISEASES OF THE NERVOUS SYSTEM, HARVARD UNIVERSITY.

As the problems suggested by the question before us are mainly clinical, I have thought that the best contribution I could make would be by collecting the unpublished cases occurring in the practice of Boston surgeons, leaving it for the referees to deal with the published cases from the same source.

With this intention I sent around a circular asking for cases of oöphorectomy done principally on account of general nervous symptoms. If the circular had been more liberally worded—in the terms of the question on our programme for example—it might have called out a larger number of cases, but the fact that the gynecologists of the city, with but three exceptions, answered that they had had no experience of the sort indicated,[1] is of decided interest as showing the general estimation in which the profession in Boston holds the operation for the removal of normal ovaries on account of nervous symptoms, or even of diseased ovaries except in response to distinct local indications.

It is certainly true that with our increased and increasing knowledge of neurasthenia and its treatment, there has grown up a distrust of the theory of specific reflex causes and of royal roads to cure, a distrust well indicated by the approval with which Dr. Goodell's widely read paper of two years ago was received. A year later, Dr. Starr,[3] of New York, made an admirable and thoroughly scientific argument in the same line, relative to the discussion upon Dr. Stevens's sections of the ocular muscles.

[1] One or two other physicians had already published cases of similar kind to those here given, as will be noted below.

[2] Medical News, 1889.

[3] Medical News, 1890.

But we should not, for the sake of the greater, forget the less. If we feel bound to enlist ourselves with vigor in behalf of the most rational view, we should not forget the facts that make for the other side, and the chief interest to me of the group of cases here collected is that they furnish some of these facts.

It is not always possible to estimate the share that a peripheral irritation has in causing neurasthenic symptoms; it is not always possible to treat the patient under the most favorable conditions; finally there are nervous systems which are not easily reached by other treatment but can be given a new tone by some striking influence. Perhaps for some of these, hypnotism or some other form of treatment by suggestion would do as much good as oöphorectomy. In two of Dr. Johnson's cases, for example, the patient improved a good deal, though only a mock operation was done. But the physician must use his most conscientious and enlightened judgment in each case, not forgetting that each patient stands for herself and not for an average.

Finally, we should not permit ourselves to be too much controlled by sentimental considerations in dealing with the question of "unsexing" the patient. The function of child-bearing is not the only or most sacred function of every woman.

No one has a right to remove the ovaries for nervous symptoms until he has convinced himself by thorough study, both preliminary and with regard to the case in hand, that it is the best thing that he or anyone else can do under the particular circumstances. If, however, he has convinced himself of this, and if he is convinced that he is not misled by impatience or natural bias, it is equally true that he has no right to omit advising the operation.

I have reports of twenty-four cases of oöphorectomy. Eleven of them were contributed by Dr. F. W. Johnson, eight by Dr. John Homans, and five by Dr. J. W. Elliot, two of the latter being also under my care.

Eight of the patients appeared to have been benefited by the operation, eleven were not benefited, two died of some other cause rather too soon to make it worth while to include their cases. This proportion of eight favorable to eleven unfavorable cases is, of course, of no statistical value, for we all know of cases enough where ovariotomy has been done in patients where nervous symptoms were present, though not on account of these nervous symptoms, and without bene-

fiting them. Possibly one cause of this may have been that the patients were not provided with the important factor of expectancy of good, for certainly this is a factor which the results of hypnotism and other "suggestive" treatments ("mind cures" etc.) show to be of immense importance.

Unfavorable results of serious character followed the operation in only three cases, although in a number of others the nervous symptoms were temporarily worse or symptoms like those frequently attending the menopause were induced. Of the three unfavorable results, two consisted in maniacal outbreaks of temporary duration, and one in an increase in the number of epileptic attacks. It is, however, only four months since the operation in this case was done.

Dr. A. T. Cabot has told me of two other cases occurring in his practice where ovariotomy, which was not done for the sake of nervous symptoms was followed in one case by melancholia of many months' duration and in the other by a shorter attack of mania, ending, after three days, in death. In the latter case the patient had shown delusions and other mental symptoms, before the operations.

As such conditions occasionally follow other operations, though especially in those in the genital tract, it would be hardly fair to attribute them to the loss of the ovaries in itself. Dr Johnson has told me that the only other case that he had seen occurred after an operation on the broad ligament.

In three other cases of the group here presented, insanity came on a longer or shorter time after the operation. It was, however, afterward learned that mental symptoms had been present before the operation in every case.

In one of Dr. Homans' cases adhesions within the peritoneal cavity consecutive to the operation seemed to be the cause of considerable pain, which was increased by walking. After about a year, the patient had a sudden sensation as of something giving way, and after the soreness subsided she was able to walk better.

In all the cases except one there were some signs or symptoms to call attention to the pelvic organs, and yet no such condition was present there as would have furnished any sufficient surgical reason for operation.

The symptoms of chief importance were of a neurasthenic character or consisted in dysmenorrhœa and local pains, local, but prob-

ably on a basis of the irritable weakness that we call neurasthenia. In three cases the reduction of uterine displacement, which had seemed impracticable previously, was made possible by the removal of the ovaries.

The majority of the ovaries and tubes in these cases were either perfectly healthy but the nucleus for a certain amount of peritonitis, or they were at most slightly enlarged or more dense than usual, or the seat of retention cysts or dilated follicles—conditions liable enough to give rise to pain at menstrual periods, it is true,[1] but not likely to be important causes of serious symptoms, except in the presence of a neurotic taint.

In some of the cases of this class it seemed almost certainly the bringing on of the menopause which induced the favorable result.

It is this view which has been held to afford a justification for the occasional removal of ovaries which would be called strictly normal, and objectionable as it is to remove them if still capable of producing ova, yet it cannot be stigmatized as being absolutely unjustifiable.

The eight cases in which well-marked improvement occurred were briefly as follows. It should be said that the operation in one of them was done only six months ago, and in another only ten months ago, so that in these cases, and possibly in some of the others, the nervous derangement, hitherto latent, may reassert itself.

CASE I.—This was the case of a young woman of eighteen, the youngest on the list. The operation was done by Dr. Homans, and the case—a very important one—has been reported both by him[2] and Dr. Goldsmith.[3] I should not refer to it here but for the fact that Dr. Homans has kindly given me new information, which brings the history up to seven years after the operation, at which time the patient died suddenly with intense pain in the head and convulsions, having remained well until then. It was a case of so-called moral insanity, of eleven years' standing, with outbreaks, especially at the menstrual period, of extreme violence. She was intelligent, but at times utterly uncontrollable, and had been the inmate of several asylums, in one or another of which she seemed likely to spend her life. The improvement after the operation was so great that she soon went home to live, and after a time was able to support herself, which she continued to do until her death.

[1] This is Dr. Johnson's opinion, after a careful study of his patients. Dr. W. F. Whitney (cited in the Boston Medical and Surgical Journal, vol. cxxiv. p. 34) also speaks of the relation of retention cysts and painful menstruation.

[2] "Three Hundred Laparotomies for Various Diseases," Boston, 1887.

[3] "A Case of Moral Insanity." Amer. Journ. of Insanity, Oct., 1883.

Dr. Johnson also operated on a patient of eighteen, a twin, with undeveloped uterus, who was neurasthenic and childlike. I do not count this case on the positive side, because the improvement did not begin for three years, though there are several reasons for attributing it to the operation, but the case is of interest because the patient developed physically and mentally, and from being childlike in appearance, manner, and interests, she became more womanly and mature. There was a marked gain in flesh, as often occurs.

CASE II. [Dr. Johnson].—Single, thirty-one years old. Symptoms: Dysmenorrhœa, pain in the left ovarian region, generally of a burning character, constipation, increased frequency of micturition, general neurasthenic condition. Physical diagnosis: Retroflexion, with disease of left ovary and tube. Family and personal history: There had been phthisis and insanity in the family, and the patient herself had suffered from hip disease from her seventh to her eleventh year. Operation, November, 1887. Removal of left ovary and tube, both of which were adherent. The right ovary was left behind, although it seemed larger than normal. Pathological examination [Dr. W. F. Whitney]: Chronic peritonitis, but the tube and ovary substantially normal. Subsequent history: Gradual but important gain as regards nervous symptoms. A year and a half ago the patient married and has had a child. She is now doing well in every respect, and has gained forty or fifty pounds in weight. The pain and head symptoms are much relieved.

CASE III. [Dr. Johnson].—Single, twenty-nine years old. Symptoms: Severe dysmenorrhœa for three years past, with general nervous exhaustion. When seen by Dr. Johnson she had headaches, pain in the back, morning fatigue, constipation, and other signs of nervous weakness. She had attacks of hystero-epileptic character, in which she would lose the use of her lips, and had lost consciousness, each attack being followed by prostration of three days' duration. The family history showed that phthisis had been prevalent and that there had also been family worries. Operation, January 31, 1888. Removal of both ovaries and tubes. Pathological diagnosis [Dr. W. F. Whitney]: Thickening of the peritoneal sheath, with retention cysts, and dropsical condition of numerous follicles. Result: After the operation symptoms of maniacal excitement. The hystero-epileptic attacks have never returned since the operation. Finally, gradual improvement. After two years the patient was able to return to work. On the whole, there has been great improvement, but not complete recovery. The patient has not been heard from of late.

CASE IV. [Dr. Johnson].—Single, thirty-eight years old. Symptoms: Four years ago nervous prostration; never very strong; a school-teacher by profession. She came to Dr. Johnson complaining of intense pain in the left leg and thigh, shooting up from the sole of the foot the whole length of the leg and thigh, the pain being increased by coughing and laughing, also by a

movement of the bowels; very neurasthenic, very constipated. Physical diagnosis: Retroversion, with probable affection of the left tube and ovary. Every sort of treatment was thoroughly tried from July, 1887, to November, 1887, without improvement. Was seen in consultation by Dr. S. G. Webber, who recommended operation, which was done. Operation, November 23, 1887. Both ovaries and tubes removed. Pathological diagnosis: Chronic peritonitis, but the tubes and ovaries healthy. After the operation the uterus stayed in its proper position. Subsequent history: April 15, 1888, the patient reported by letter that she was getting on very nicely, and only suffers from general nervousness. Her spirits, which had been very much depressed before the operation, had greatly improved. Somewhat later, she wrote that she was constantly gay and lively. She gained thirty pounds in weight in five months. On June 23d, of the same year, the sciatic pain was reported as still present (felt in the sacral region and running down the leg, but only when standing). Since then she has reported that she has completely recovered and has gone back to teaching school. Would not be known for the same person.

CASE V. [Dr. Johnson].—Married, twenty-six years old. Symptoms: Intense headaches of neurasthenic character, with some other neurasthenic symptoms and dragging sensation about the pelvis. Family history: Phthisical tendencies; father extremely nervous. The patient had had headaches even as a child, had been married four years, and had two children. Physical diagnosis: Retroflexion and small fibroid in posterior wall of uterus; laceration of cervix; ruptured perineum. She had had an operation for the cervix and perineum at Denver, but found only temporary relief, and no relief from the headaches. Dr. Johnson had her eyes and pharynx thoroughly examined and treated, as possible causes of the headaches. There was some improvement, but the symptoms soon returned. She had her teeth pulled, without relief. Was seen in consultation by Dr. S. G. Webber. The retroflexion was overcome by packing, which relieved the backache so that she was able to walk without pain. Operation, November 12, 1890. Both ovaries and tubes were removed. Pathological diagnosis: tubes normal, and ovaries practically so (Dr. W. F. Whitney). Results: At first she lost ground in all respects; the headaches and backaches increased; she lost flesh and strength; her husband became frightened, and thought she would go insane, but in three or four weeks she began to improve, and now she is better in every respect and is able to ride a bicycle.

CASE VI. [Dr. Johnson].—Single, twenty-seven years old. Symptoms: A neurotic patient, Jewish by race, and of a neurotic family. She was a brilliant person, but had suffered from migraine since childhood, as her mother had before her. She was a good student. The headaches increased in frequency, and finally were of almost daily occurrence. Dysmenorrhœa was so bad that an immense amount of morphine was used from time to time, and insanity was feared. Dr. Myles Standish examined her eyes and found insufficiency of some of the ocular muscles, and operated, securing relief for two

weeks only. She was then seen in consultation by Dr. W. N. Bullard, who advised removal of tubes and ovaries. The only physical sign of consequence was tenderness in the neighborhood of the left ovary. Operation, April, 1891. Left tube and ovary adherent. Both tubes and ovaries removed. Pathological diagnosis: Very little found that could be called pathological (Dr. W. F. Whitney). Results: The night after the operation the patient had had a hystero-epileptic attack with opisthotonos, lasting for six hours. Six weeks later she wrote: "I am feeling very well, only two or three headaches, and these lasted only a day and a night. This is such a change from the headaches of six days' duration that I am much pleased. I have gained rapidly, and am much stronger than I expected to be at the end of six months." The local symptoms in this case were very slight.

CASE VII. [Dr. Homans].—Mrs. S., thirty-six years of age; one child. Symptoms: Pain in left side of pelvis; offensive discharge. The patient was worn and pale-looking. She had nervous prostration when eighteen, and got into the morphine habit. One ovary prolapsed and tender. Operation June 23, 1889. Ovaries somewhat atrophied, but otherwise normal. Results: Marked gain in flesh and strength and general tone. Menstruation continued, and became more frequent. She gave up the morphine habit.

CASE VIII. [Dr. Elliot and Dr. J. J. Putnam].—Miss. B., thirty years old. Symptoms: General ill-health, nervous weakness, and constant headache for nearly two years; sleeplessness, with bad dreams, sense of weariness, and aching of the whole body; local symptoms moderately severe. Sister neurasthenic to some extent. Physical diagnosis: Enlargement of ovaries, tenderness, and prolapse; enlargement, retroversion and tenderness of the uterus. Operation, April, 1885. Removal of the ovaries and tubes. Pathological diagnosis [Dr. W. W. Gannett]: Ovaries enlarged and cystic. Result: Continuation of the headache for three months or more, after which gradual improvement. The same may be said of the other symptoms. No return of the menses. Patient, who had been dragging herself about in great distress for nearly two years, returned to work six months after the operation, and although she has been obliged to be careful, she has improved steadily ever since, and says that she was never in such comfortable condition as since the operation. She has worked regularly and with pleasure, and supports herself. This case seems certainly one where a too rigid conservatism would have worked to the patient's disadvantage. Every kind of general treatment that the circumstances allowed was carried out faithfully, but without effect. The present result is in every respect satisfactory.[1]

[1] The experience of Boston surgeons already published embraces the following cases:

1. Dr. E. W. Cushing: Case of melancholia and masturbation, in a negress; result, cure, which has persisted to the present day. [Journ. Am. Med. Assoc., Chicago, 1887.]

2. Dr. John Homans, loc. cit.: Four cases without improvement.

3. Dr. F. W. Johnson: Case of salpingitis, displacement of uterus, with adhesions, prolapse of ovaries (afterwards found to be disorganized with retention cysts), abdominal pain, dizziness, frontal and occipital headache, dyspepsia, constipation. Recovery. [Boston Med. and Surg. Journ., vol. cxxiv. p. 33.]

Finally, I have one case of castration in the male to report upon:

The patient was thirty-eight at the time of the operation, which was done three years ago, the case not being under my care at that time. He had had since childhood, and especially since a severe blow on the head, a very unbalanced nervous system, and had for some years been so badly addicted to drinking and other excesses, and became so irresponsible, that he was sent for a time to an asylum. Previous to the operation he had again fallen into drinking and had become excessively lascivious, and on this account and by his own urgent request the operation was done. By his account the testicles were found enlarged and hard. He has remained unbalanced to a considerable degree, and of late has been a cause of great anxiety; but the special symptoms for which the operation was done—the dipsomania and the lasciviousness—seem to have disappeared entirely up to the present time, and he has been quieter and more reasonable in temperament.

In one or two of Dr. Johnson's cases the general nervous symptoms were worse for a time after the operations, though they afterward grew less.

In view of the terms of our discussion it would not be worth while to report this fact except that it strengthens somewhat the probability that the operation often acts not so much by removing an active cause of irritation as by bringing on a premature menopause. As a matter of fact, the favorable result, where this occurred, often failed to appear for a number of months, and was said to be frequently preceded by nervous symptoms such as accompany the menopause.

In conclusion, I do not claim that the favorable results reported in these cases could not have been brought about in some other manner, but only that they were, or seem to have been, brought about in this way, and that the patients are not reported as regretting the operation.

My patient is still, after several years, enthusiastic as regards the benefit that was done her.

My own opinion is as follows: When ovarian or uterine disease of slight or moderate amount is associated with marked nervous symptoms, whether these are of the nature of unusual local pain, or of a more general character, it is rarely the case that the local disease is alone at fault, and the physician should look carefully for other signs of the main trouble in the nervous system itself. It is so often found, in practice, that by invigorating the general nervous condition the patient can be made comparatively insensitive to local irritations, that, before deciding on a step that may lead to bitter regret and disap-

pointment, the physician should omit no other means for accomplishing his aim which study, determination, and skill can secure, and even if he fails he should remember that his chance of success through oöphorectomy is not of the best.

It should be especially borne in mind that the element of personal temperament and personal influence plays an important part in the treatment of neurasthenia and mental disorders, so that some new physician may succeed where many have failed, or that anyone may do better than he believed possible if he chooses the best method and relies upon it with sufficient persistence. The new light which the investigations into hypnotism and kindred subjects have thrown upon the pathology and therapeutics of the nervous system indicate that when oöphorectomy cures neurasthenia it sometimes does so by influencing cerebral processes not ordinarily concerned in active consciousness, and there is always room for hope that some other and less objectionable means can be found of exerting this same influence.

All this the physician should conscientiously say to himself, but, having done so, he should with equal conscientiousness recall the cases in which oöphorectomy was the agent that restored many patients to health, and should look upon it as another and valuable string to our bow. As a rule, the bad nervous cases (epilepsy, hystero-epilepsy, well-marked hysteria and neurasthema, or insanity) are not permanently benefited, yet such cases as No. 1 [Dr. Homans'], shows that even this cannot be absolutely asserted. The best cases for operation are doubtless those where the symptoms are most nearly "reflex," and then—as Dr. Elliott has especially pointed out to me—where the inducing of uterine involution may relieve the patient of painful and exhausting irritations which, in view of the patient's health and circumstances, it may be impracticable to cure by other means.

DISCUSSION.

DR. MITCHELL: I had the honor of suggesting this subject as one for consideration at this meeting, and, of course, it is natural that I should be called upon to say something. Naturally, after having heard Drs. Lusk, Sinkler, and Putnam, I have but little to say. There are some criticisms which occur to a man of my years, which may not have suggested themselves to the authors of these papers.

First, as to these papers: I think it will occur to some of you that the great mass of material in the way of cases presented by Drs. Lusk, Sinkler, and Putnam, are nearly all from irreproachable people. The great mass of material comes from operators who were careful, thoughtful, and are among the best names we know in the operative science in which they are distinguished. What we want to have, and what is most difficult to get, is the statistics of the reckless operations which many of us know to prevail, of which a great many of us have seen the victims, and of which I am in constant fear for that form of woman who invites by her temperament, and perhaps her disease, the removal of her ovaries. I have seen a great many cases where the ovaries ought never to have been touched. I hear of statistics of normal oöphorectomies whose number I hesitate to mention. Among the most reckless will be, I fear, the women operators of the future. I judge from my experience of the past. It is chiefly toward the young operators that my criticisms are directed. If what has been said here, what has been countenanced by such a body of men as I see here, can have any influence with this class of people, it ought to secure greater thoughtfulness and more general medical conscience about this matter. I ought also to say, when thus criticising some of my surgical brethren, young and old, that we should be a little careful and have some charity. Every new medicine, every new operation, is apt to induce excesses either in medicine or surgery. After a while these cure themselves, often after heavy cost, perhaps in consequence of the exhortations of such bodies of men as we have here to-day. Take, for example, the introduction of the bromides. There is not one of us who has not seen very serious results from their use. At last experience began to protest, and now it is rare to see bromides injuriously affecting cases. They were hurtful only because the men who used them did not know what they were about.

These cases of ovarian loss have not gone on long enough to give really remote histories. We want to know what becomes of women, operated on at eighteen to twenty, ten or fifteen years afterward. If you collect the histories of such cases as thigh amputations, ten or fifteen years afterward, as I have done, you will find remarkable changes in the nervous systems of those who were operated on, and this source of study amply rewards care.

I can say that during a long professional experience, I have only in fifteen cases felt myself forced to call upon the surgeon for removal of the ovaries. As to these, I will say that there was no death. I never have seen a death in a case of mine, and I think that one fair reason in regard to this, and to the success of a good many operations done upon my patients, is not alone that we have improved very much in the "failure to produce death" by operations, but also that every case which I submitted to the surgeon I previously carefully prepared for the operation. One of the criticisms I have to make upon the surgeon of to-day, and especially of the surgery of oöphorectomy, is that where you find one man as careful as Lusk, you will find a dozen who will see a patient to-day and in a week will operate. I say here that the practical abolition of the death penalty in surgery has produced an

amount of temptation in the surgical mind which is responsible for a good deal of the mischief of which I have now been speaking. It has made men, if not reckless and indifferent (I do not think either phrase ought to be applied), too ready to operate, and to operate without medical consultation. I could mention many cases where quite inexperienced men have done oöphorectomies without any consultation with any other living man. I do not think this operation should ever be done by a surgeon without consultation with a physician, and if the physician says wait, then the operator should wait. There should be more consultations and more seriousness.

Again, there is the aspect of the case which Dr. Sinkler has stated in speaking of one of my own patients. I want to speak of this, because it applies not only to young men but also to old and thoughtful men. If men like Goodell and Sims and Lusk can make mistakes, it should make younger men extremely careful. I will only speak of four cases. All of these cases came to me from California. All of these were young married women from the better class of life and of sufficient means. Three were singularly good-looking women. These four women came here condemned in California to lose their ovaries. In one case my friend Dr. Goodell believed that no other cure was possible for this woman. I cured them all. They are all happy women to-day, and it is three years since the last one was cured. They have all had children since, and are able to do everything that a woman should do. This ought to be a lesson; it should cause us to reflect. I have no doubt if the ovaries had been removed they would have gotten well and had reasonably happy lives. I prefer to get them well without crippling them in any way.

DR. W. T. GAIRDNER, of Glasgow: I only intend to mention one case. In Scotland I do not think we are very familiar with the reckless surgery alluded to, but, nevertheless, I have no doubt that the necessity for caution exists. I was peculiarly pleased with the tone of Dr. Lusk's paper. It satisfies my mind completely, and if I were to express what is the state of my own mind I could do it in no better way than to indorse almost everything in Dr. Lusk's paper.

There is one striking and almost epigrammatic case which came within my own knowledge long ago, and which speaks volumes in itself. I had the opportunity of knowing a case many years ago who consulted, among others, the late Sir James Simpson. It was before the days of these operations referred to to-day, and therefore the question of excision of ovaries did not occur, but the fact that it did not occur has not removed from my mind the idea that if the same circumstances had been presented to certain surgeons in the present day, or at any time within the last ten years, that question would have been raised. The history of that young woman was this: She was always what I suppose would be called neurasthenic, and she is so now, but she suffered particularly at the menstrual periods to a point which cannot be expressed by anything else than positive agony, and this of such a character that if it had gone on to embitter her life to middle age (she remaining unmarried)

she herself would have raised the question of doing almost anything to get rid of it. She married at twenty-five. Her husband witnessed one, one only, of these extreme—indeed, to him and to her, terrible attacks. She became pregnant, and from the time of becoming pregnant her whole life since has been entirely free from any of the former trouble. She has borne nine children, and is an excellent mother. This is an epigram in itself, and I think a case of that kind before the mind of everybody who is placed in contact with the question of excising the ovaries of an unmarried woman, and even of married women, will be of service.

DR. CHARLES CARROLL LEE, of New York: I will be brief. I think it would be impossible to summarize more fully than has been done by Dr. Lusk, and Drs. Sinkler and Putnam, the general outcome of this subject, and all that anyone can do now is to give as briefly as possible the view to which he has come, the result at which he has arrived, as the legitimate outcome of his own experience. I, when asked this summer at Newport by my friend Dr. Lusk if I had any reliable statistics on this subject, departed from my usual modesty and said that I had. I did so because eight or ten years ago, happening to be in England, I was struck by the fact that all of my English friends who were interested in laparotomy seemed to be full of the surgical aspect of the subject, and to know nothing about the ultimate results to their patients. I make one exception to this, namely, Dr. Keith. That was nearly ten years ago. I began then—having already had considerable experience in laparotomy (cases to some of which I now look back with shame and mortification)—to tabulate the records, and to keep up with the records, so well as I could, by constant communication by letter in circular form which I issued every year to all of my patients upon whom I operated. I have tabulated 120 to 130 cases of removal of ovaries which I have done for what I thought to be legitimate cause—removal either for local disease, or disease of the nervous system. I will state very briefly as the outcome of this large correspondence that I have yet to report—and I am mortified to have to say this after the amiable reprobation and denunciation to which I have been obliged to listen by my neurological friends—a single case of benefit after a lapse of five years, where the removal of the appendages was done for neurotic conditions. I have yet to see, in spite of what my distinguished friend has said just now about the lack of preliminary examination and consultation in cases where there was distinctly ascertained structural disease of the appendages, a single case, carefully observed and carefully attended, that was not benefited. I would therefore say, in brief and in fine, that the removal of the uterine appendages is not only legitimate, but is a necessity in all cases in which a permanent structural lesion has been made out, and this change, I think, can be accurately made out. Certainly you can diagnosticate pyosalpinx accurately, and certainly it never gets well without amputation of the appendages. Certainly conditions of hæmato-salpinx constantly get well. Ovaritis constantly gets well without removal of appendages. By limiting cases in which this operation of laparotomy should be

done to those of decided structural change, you get results from the operation, if properly and carefully done, which are just as gratifying to the operative surgeon, in spite of his drawbacks and his tendency to operate sometimes improperly, as in cases of that kind which have passed through the most distinguished neurological hands. When it is done within proper limitations I think it one of the most beneficent of modern surgical operations.

DR. WATHEN: I came here neither expecting nor prepared to say anything this morning, but to listen to the very interesting and practical paper of my friend, Dr. Lusk. I have been very much interested, not only in Dr. Lusk's paper, but also in the papers which have followed, and in the discussions upon these papers. I am unable to discuss this question from a medical standpoint because it has been a good many years since I have had experience in any department of medicine or surgery except that relating to operative work in gynecological, abdominal, and pelvic surgery. I think this Society deserves thanks for having brought this subject before the profession of this country. What goes forth from a society of this sort impresses upon the minds of the medical profession of this country, and other countries, practical lessons that will tend to control them in excesses of any kind. That there have been excesses in abdominal and pelvic surgery no one knows better than the conservative abdominal surgeons. There are but few of us who have not in our early experience removed the appendages where we now feel perfectly sure they should not have been removed, and where we would never again be induced, in a similar case, to consider the propriety of removing the appendages. There is too much pelvic surgery done, and too many men are doing it—men who know too little about the diagnosis, the pathology, and the surgical technique of these cases. And a great deal of harm results in consequence. I can hardly conceive of any instance in which ovaries and tubes, considered in a physical examination as normal, should be removed—it matters not what may be the neurotic condition of the patient.

Again, I believe that ovaries and tubes diseased to a certain extent should not be removed in frequent instances, even though a laparotomy is necessary. Laparotomy in pelvic surgery may be a conservative operation, and it may be one that ought to be done, and still we may not be required to remove the appendages, but to protect them, to bring them into a healthy condition and save them. If the uterus is retroverted or retroflexed, and bound down by adhesions causing distressing and persistent reflex disturbances with more or less adhesion of the ovaries and tubes, and probably some small cystic degeneration of the ovaries, the expert operator may do an operation almost free from danger, restore the uterus to its normal position, separate all adhesions, if the ovaries are cystic open them and remove the cyst, without injuring the ovaries. If one tube is diseased and the other healthy, remove but the one. Bring the uterus into its normal position and by the proper surgical procedure keep it there. Restore the woman to health and place her in a position where she can more readily bear children than before the operation was performed. I am frank to acknowledge that in my earlier experience I removed

ovaries and tubes that ought not to have been removed; but now I am trying to make amends by apologizing for this, and by insisting upon the medical profession opposing all such reckless procedures, and advising the practice of *conservative surgery of the pelvis.*

DR. LUSK: I think there is absolutely nothing to be said; we all seem to occupy exactly the same ground. My own point of view is this: that at the present time there are a certain number of cases that I do not know how to treat any better than by taking out the ovaries and tubes, but there are so many cases that I can cure without the operation that I would have supposed it impossible to cure five years ago, that I am in hope that next year, perhaps, I may still further reduce the number of cases in which the operation is called for. What we need especially is help from the general body of the profession. There has been a disposition on the part of the so-called pelvic surgeon (he belongs to a class by himself) to sneer at everybody who states that it is possible for patients to get well by means other than incision through the abdominal wall, and it is about time that the profession, as a class, turn around and assert their rights, that they shall state to these gentlemen that they are perfectly competent to make a diagnosis, and that when they say that they have cured their patients by other means, that their word is just as good as the pelvic surgeon's, who blows his horn and tries to drown all contrary experience. And then, on the other hand, it seems to me necessary that we should spread abroad the idea that the performance of a laparotomy and the removal of ovaries and tubes is not a stupendous form of surgery. I am a general practitioner, like Dr. Lee. Circumstances, however, have brought a certain number of cases into our hands, and operations have been followed by just as good results as have occurred to the most distinguished of the pelvic surgeons. As soon as the removal of the ovaries and tubes is looked upon by the profession as other forms of minor surgery, from that time it will be possible to get something like sense in the discussion and in the study of this subject.

NERVE-STRETCHING IN INVETERATE TRIGEMINAL NEURALGIA.

By JAMES STEWART, M.D.,
PROFESSOR OF PHARMACOLOGY AND THERAPEUTICS IN M'GILL UNIVERSITY, MONTREAL.

In the short paper which I have the honor to read before the members of this Association, I confine myself entirely to the consideration of those inveterate cases of trigeminal neuralgia which are usually described under the name of epileptiform neuralgia. This term includes not only those cases attended by spasm of the facial muscles, but also that class of cases in which the neuralgic paroxysm comes on with great suddenness, lasts a few seconds, and persists for years in spite of all the ordinarily employed external and internal remedies. During the past two years, through the kindness of my colleagues, three cases of inveterate trigeminal neuralgia have come under my observation; and as the result of treatment in all three was fairly satisfactory, I will give a brief account of them, and afterward refer to those published cases in which a similar treatment was carried out.

CASE I. *Inveterate trigeminal neuralgia confined to the left infra-orbital branch; nerve-stretching; complete relief for thirteen months.*—A married woman, aged fifty years, first came under observation in November, 1889, complaining of severe neuralgic pains in the left infra-orbital region. Her previous health was good. There is no history of neuroses in her large family connection. The first paroxysm of neuralgia came on twelve years previously, and was attended by a profuse flow of saliva. For a period of about two years she had no recurrence of the attacks, but during the past ten years she had many attacks daily during the winter months of these years. She was entirely free during the summer months. During all these years she had been perseveringly treated by many different physicians, but with very little relief. When I saw her she was willing to submit to any measure whatever to purchase even temporary relief from her cruel suffering. I advised stretching the nerve, and Dr. Shepherd, of Montreal, kindly consented to undertake the operation, which he performed in December, 1889. She remained entirely free from pain for

thirteen months after the operation. In January, 1891, the pain returned in the same spot with much of its old-time severity, but only lasted a few weeks. For the past six months she has remained entirely free. (Reported by Dr. Weagant, of Dickinson's Landing.)

There can be no question that the operation in this case was eminently beneficial, complete relief lasting for fully thirteen months after its performance.

CASE II. *Epileptiform neuralgia of the right infra-orbital nerve of four years' standing: stretching of the affected nerve, followed by complete relief for fourteen months.*—This patient, a woman aged sixty-five years (a patient of Dr. Ross), was never affected with neuralgia until after her sixty-first year. The family history did not show any tendency to neurotic troubles. Her previous health was fair. She had, however, borne more than an ordinary share of the world's cark and care. For a period of four years she has been troubled with severe darting pains in the region of the right infra-orbital nerve, and for several months before the operation the paroxysms had assumed an extremely severe form. For hours, and even for a day or two at a time, she was not infrequently compelled to remain perfectly quiet in the endeavor to lessen the number of attacks. During this time she could neither eat nor speak without the occurrence of a paroxysm. The severer attacks were usually accompanied by twitching of the muscles of the same side of the face. All the usually employed remedies in this disease were successively resorted to, with little or no relief. In this rather hopeless state she readily consented to submit to any operation that was even likely to bring partial relief. Dr. Shepherd stretched the right infra-orbital nerve in February, 1890, and, with the exception of one severe paroxysm a few hours after the performance of the operation, the patient remained entirely free from pain for a period of fourteen months. After this she had, on several occasions, slight recurring attacks at considerable intervals, but the intensity of the pain never reached what it did in the period previous to the operation.

This patient died in August of the present year from enteritis.

CASE III. *Severe neuralgia of the right infra-orbital nerve: nerve-stretching, followed by four months' relief.*—I am indebted to Dr. Buller, of Montreal, for the details of this case. The patient, a woman, eighty years of age, but looking much younger, being well nourished and of fresh complexion. Fifteen years ago she received a severe injury to the right shoulder, involving the brachial plexus, but from which she appears to have entirely recovered. She, however, dates her facial neuralgia from this period. The pain is described at times as dull, but usually of a sharp, darting nature, and is attended by extreme sensitiveness of the inner part of the right upper alveolus. All the teeth in the right upper jaw have been removed, but with little or no beneficial result. The pain, though chiefly located as described, at times affects

the whole side of the face, brow, and temple. The supra- and infra-orbital foramina are rather more sensitive to pressure than the surrounding parts. Seven years ago she had an attack of subacute glaucoma of the right eye (painful side), for which an iridectomy was performed successfully, inasmuch as the tension has remained normal ever since, and vision, although defective, improved after the operation. The left eye has at no time shown any signs of glaucoma. On January 12th of the present year Dr. Buller says: "I stretched the infra-orbital very forcibly, but as far as I could judge, without any solution of its continuity. Four days after, on examination, the wound was found completely healed, and all pain had ceased from the date of the operation." Her attending physician reports at this time complete loss of sensation and reflexes on the right side of the tonsil, uvula, and soft palate. Twenty-five days after the operation he writes: "The operation was very successful as far as relieving the pain, but the loss of sensation already referred to still persists, and, in addition, there is a complaint of a wooden sensation in the region of the face corresponding to the distribution of the infra-orbital nerve. These parts are also distinctly anæsthetic." In this case, four months after the operation, there was a return of the old neuralgic pain. Six months after the operation Dr. Buller carefully examined the patient and reports: "The stiff, board-like feeling she complained of in the right upper lip and adjacent parts has disappeared. The paroxysms of pain are less frequent and less severe. She speaks of them as being quite bearable now in comparison to what she formerly suffered."

In the three cases reported we had complete relief, lasting in one for fourteen months, in another about twelve months, and in the third for four months. These results, although not of a very enduring character, still are sufficiently pronounced to much more than counterbalance the slight danger and distress attending the operation performed. In each case the patient would willingly have purchased even a few weeks' relief at greater cost.

A large number of cases of trigeminal neuralgia treated by nerve-stretching have been reported, but, unfortunately, the vast majority of these reports are worthless as an aid to settle the question as to the permanent value of the operation. It is very exceptional to find a case of nerve-stretching reported where very marked or complete relief has not taken place, and, as the great majority of these cases are reported within six months after the operation, they go to swell the list of alleged completely successful cases. There is no doubt, I think, that the great majority of these relapse, are not again reported, and erroneous conclusions as to the success of the procedure drawn.

I have endeavored to obtain the result of nerve-stretching in all

those cases in which the state of the patient was reported nine months and upward after the operation. It is surprising how few cases observed for this length of time are obtainable. Fully 90 per cent. are reported before six months have elapsed. In Dr. Chandler's and Professor Agnew's collections, with the exception of one case, the longest time a patient was under observation was seven and a half months.

I have only been able to find a record of eleven cases in which the observation of the patient extended beyond nine months, exclusive of the cases I have reported. Mr. Walsham, of St. Bartholomew's Hospital, reports three cases of complete relief lasting three years, fourteen and thirteen months, respectively. Grainger Stewart reports one that remained well one year after, and the late Mr. Spence reports one nine months after operation still free from pain. Lefort reports one case where relief lasted more than one year, and Lagrange three extending over three years, one extending over two years, and one over eighteen months.

It would be very interesting to have a report on all cases operated in from one to two years after the operation. There is no reason to doubt that the percentage where permanent relief is obtained is very small, probably not more than 5 per cent. It is contended by some surgeons that the relief obtained is not sufficient to counterbalance the annoyance of the operation to the patient. In judging this question, we must take into consideration the fact that in the great majority of cases we obtained marked relief for a few months, a relief which is a great boon to the distressed patient; and, further, the operation can be repeated with the probability of a continuance of relief. If repeated nerve-stretching fails eventually to give the relief demanded, other but more severe operative measures can be resorted to.

These are the performance of neurectomy, and in the case of the infra-orbital the removal of Meckel's ganglion, and ligature of the common carotid. Dr. Fowler (*Annals of Surgery*, 1886) has collected 83 cases in which portions of one or more of the branches of the fifth nerve have been removed. In fully 25 per cent. of these cases relief from pain lasting a year and upward followed. In Wagner's table (*Archiv. für Chirurgie*) of 135 neurectomies, 18 complete cures are reported, and in 20 cases relief lasted from one to three years. There are several other cases of neurectomy reported since Fowler's

and Wagner's tables have been published. Including these, I have been able to collect in all 250 cases, and I think I am safe in saying that in fully 20 per cent. we have relief extending from one to three years, and probably 10 per cent. of complete cures. The showing from neurectomy is, therefore, considerably better than from nerve-stretching, but it must be remembered that neurectomy is an operation not devoid of danger.

In Wagner's collection there were six deaths; in Dr. Fowler's, no fatal results are reported. As Dr. Wagner's cases occurred in pre-antiseptic days, the mode of operating probably accounts for the unfavorable results in so many cases. Nerve-stretching is a mild operation as compared with an extensive neurectomy, and should, I think, be always preferred to it. Another important reason for preferring nerve-stretching as the preliminary operation is that if it fails it may be repeated several times, while if an extensive neurectomy is first performed, no operation except the grave one of ligaturing the common carotid can be performed. As the great majority of cases of epileptiform neuralgia are due to central mischief, it follows that after the failure of an extensive neurectomy neither nerve-stretching nor a further neurectomy is possible.

From our present experience of nerve-stretching in inveterate trigeminal neuralgia, I believe the following conclusions are justifiable:

1. Nerve-stretching gives either complete or great relief in the majority of cases.

2. Relief is not permanent in more than 5 per cent. of cases.

3. If the pain should return, the operation should be repeated, even several times, before resorting to a neurectomy, or ligature of the common carotid.

4. If the pain is not strictly and always limited to one branch of the nerve, several branches should be stretched.

5. As relief does not always immediately follow the stretching, a second operation should not be undertaken until some time has elapsed.

ON THE DISEASES OF THE KIDNEYS POPULARLY CALLED "BRIGHT'S DISEASE."

By FRANCIS DELAFIELD, M.D., LL.D.,
PROFESSOR OF MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK.

Our notions concerning the nature of diseases and of their treatment are greatly influenced by names and classifications. So, as our knowledge becomes more accurate, it is important, as fast as may be, to modify and change such names and classifications as have become a hindrance instead of a help.

The ordinary history of such names is that during the earlier periods of medicine some man more able than his fellows was able to group together a number of cases of diseases, to describe them plainly and to venture some theory as to their nature. Such a group of diseases then became known by the name of its describer, or by some arbitrary term. As time went on such a name acquired the dignity of use and custom, became generally accepted, and more and more traditions and classical descriptions accumulated about it, until in men's minds were established a name and a clinical picture to which, as to a Procrustean bed, they compelled their cases to correspond. With the further progress of medicine came the fresh study of the old diseases and the discovery that much could be seen and demonstrated which it was difficult to reconcile with the old traditions. Then came an unsatisfactory period during which the old name was retained as expressing a real entity, and the attempt was made to divide and classify the varieties of this entity. Lastly comes the time when the old name is retained as a popular term, but it is recognized that it does not really designate a distinct form of disease. Such has been the history of such names as "cancer," "phthisis," and "Bright's disease."

I believe that the time has fully come, to abandon the idea that there

is such a disease as Bright's disease, and to cease from the attempt to describe varieties of a disease that does not exist. When we have divested our minds of this tradition we can begin to study the diseases of the kidneys and to try to classify them.

There seem to be three ways in which we can classify kidney diseases: according to their causes, according to the part of the kidney involved, or according to the nature of the morbid process.

The attempt to classify kidney diseases according to their causes is, in the present state of our knowledge, simply impossible.

The attempt to classify them according to the part of the kidney involved, to describe tubal nephritis, glomerulo-nephritis, interstitial nephritis, and arterio-sclerosis, has been made many times. It has never given us a classification of practical use for clinical purposes.

A classification according to the nature of the morbid process is altogether the most promising.

There are three morbid processes which occur in nearly every part of the body, which produce definite anatomical changes, cause regular clinical symptoms, and call for appropriate methods of treatment. These morbid processes are: Congestion, degeneration and inflammation.

Congestion, whether acute or chronic, produces an accumulation of blood in the veins and capillaries of the part affected, causes local symptoms and disturbances of function, and is to be relieved by means addressed to the circulation of the blood.

Degeneration, whether acute or chronic, produces changes more or less profound in the parts affected; is regularly caused by poisons, by disturbances of circulation and by other diseases; produces disturbances of function according to its severity; may be itself a cause of inflammation, and can be but little affected by any treatment.

Inflammation is attended with three essential features, which may occur separately, or together: an escape of the elements of the blood from the vessels, a formation of new tissue, and a death of tissue. So we speak of exudative, productive, and necrotic inflammations.

Exudative inflammation is of short duration, leaves behind it no permanent changes in the parts affected, and can be favorably affected by treatment.

Productive inflammation runs an acute, subacute, or chronic course. It effects permanent changes in the inflamed parts. Its acute forms

are very apt to become chronic. There is much variety as to the relative quantity of exudation and of new tissue. Treatment is not very satisfactory.

The different forms of kidney disease which are commonly included under the name of Bright's disease can all be conveniently classified under the heads of—

Congestion of the kidney.
Degeneration of the kidney.
Inflammation of the kidney.

Such a classification has the merit of being simple and easily understood, of resting on an anatomical basis, and of being of practical use for clinical purposes.

I. The Congestions of the Kidney.

These are naturally divided into acute and chronic congestions. They must always depend upon causes which affect the circulation and cause an accumulation of venous blood in the kidney.

Acute Congestion of the Kidney is produced by the ingestion of poisons, by extirpation of one kidney, by injuries, by surgical operations, and by unknown causes.

It may occur in kidneys previously normal, or in those already diseased.

The most marked symptom is the diminution or suppression of the urine, but albumin and casts may be present.

Such an acute congestion is a transitory condition, but when it occurs with injuries and with surgical operations it may apparently be a cause of death.

Chronic Congestion of the Kidneys is produced by some long-continued mechanical interference with the circulation of the blood, an interference which necessarily causes congestion of other parts of the body as well as of the kidneys.

The characteristic changes in the kidneys are: swelling, or flattening of the epithelium of the cortex tubes, dilatation and thickening of the capillaries of the glomeruli, congestion and dilatation of the pyramid veins.

The urine is more or less diminished in quantity according to the intensity of the congestion. Its specific gravity is from 1020 to 1025,

but it may for a time fall to 1010, or rise to 1035. The excretion of urea is usually 10 grains to the ounce; it may rise to 21 grains. Albumin and casts are absent, or only present in very small quantities. The bad results of chronic congestion are: the diminished production of urine, and the liability to the supervention of chronic nephritis.

II. Degeneration of the Kidneys.

Degeneration of the kidney is always a secondary process, produced by the introduction into the body of inorganic poisons, or of the poisons of the infectious diseases; by the effect produced on the body by chronic diseases or vicious modes of life; or by disturbances of the circulation.

There are no changes in the kidneys except in the renal epithelium. In these cells are developed a variety of degenerative and necrotic changes.

It may happen that these degenerative changes are developed so rapidly that the bloodvessels are irritated, and there are added congestion and exudation of serum. We include, therefore, in this class both those kidneys the seat of degeneration alone, and those in which both degenerative and exudative inflammation exist, but the inflammation is secondary and subordinate to the degeneration.

Acute Degeneration of the Kidneys is found almost constantly with the infectious diseases and with poisoning by arsenic, phosphorus, and mercury. It occurs in many different degrees of severity, and so we find the renal epithelium: merely swollen and granular, or infiltrated with granules, or broken and disintegrated, or in the condition of coagulation necrosis.

In correspondence with the degree of the degeneration of the renal epithelium is the severity of the clinical symptoms.

The urine is unchanged, or its quantity is diminished, or it contains a little albumin, or the albumin is abundant with casts and red and white blood-cells.

Many of the examples of this lesion are of so mild a type that they have no symptoms except the changes in the urine. The severe forms are dangerous to life; but dropsy and disturbances of the circulation are not associated with them.

Acute degeneration, therefore, includes a well-defined set of cases,

definite in their lesions, their causes, their symptoms, and evidently not likely to be influenced by any treatment.

CHRONIC DEGENERATION OF THE KIDNEYS is produced by the same mechanical causes as those which produce chronic congestion, by chronic alcoholism and by vicious modes of life. It is, therefore, always a secondary lesion.

The only changes in the kidney are in the epithelium of the tubes, of which the cells are swollen, granular, and infiltrated with fat. But if the degeneration is due to chronic congestion there will also be changes in the glomeruli.

The quantity of urine varies at different times in the same case and also in different cases; it may be abundant, scanty, or suppressed. Albumin and casts in moderate quantities are often present, but the specific gravity is not lowered.

Such a degeneration of the kidneys has a decided effect upon the health and nutrition of the patients. They lose flesh and strength, become anæmic, and finally pass into the typhoid state with delirium and stupor. Dropsy and disturbances of the circulation are not associated with this form of kidney disease. As the kidney lesion is always secondary to some other serious morbid condition, it is often difficult to tell how much of the loss of health is due to the primary disease and how much to the change in the kidneys.

III. THE INFLAMMATIONS OF THE KIDNEY.

These are naturally subdivided into—

Acute exudative nephritis.
Acute productive or diffuse nephritis.
Chronic productive or diffuse nephritis with exudation.
Chronic productive or diffuse nephritis without exudation.
Suppurative nephritis.
Tubercular nephritis.

ACUTE EXUDATIVE NEPHRITIS.—This is an acute inflammation of the kidney characterized by congestion, an exudation of plasma, an emigration of white blood-cells, and a diapedesis of red blood-cells from the vessels; to which may be added swelling or necrosis of the renal epithelium, and changes in the glomeruli.

Of such a nephritis we may distinguish three varieties:

1. A mild form, which gives symptoms during life, but leaves no lesions in the kidney after death.

2. A more severe form, in which we find inflammatory changes in kidney after death.

3. A form characterized by the excessive production of pus-cells.

Lesions. In a nephritis of this type we should expect that the inflammatory products, the serum, white and red blood-cells, and coagulable matter from the blood-plasma, would collect in the Malpighian bodies and tubes, or infiltrate the stroma between the tubes; and that, of the inflammatory products in the tubes and Malpighian bodies, a part would be discharged with the urine and a part found in the kidney after death. We should also expect that the quantity of inflammatory products would be in proportion to the severity of the inflammation, and that an excessive number of pus-cells would belong to the especially severe forms of the disease. Still further, it is evident that, with the milder examples of nephritis, with but little exudation, no inflammatory products might be found in the kidney after death, all having been discharged into the urine during life.

As a matter of fact, the kidneys do present just such changes. In the mild cases we find no decided lesions in the kidney after death. In the more severe cases the kidneys are increased in size, their surfaces are smooth, the cortical portion is thick and white, or white mottled with red, or the entire kidney is intensely congested. If the stroma is infiltrated with serum the kidney is succulent and wet; if the number of pus-cells is very great, there will be little whitish foci in the cortex.

In such kidneys we find the evidences of exudative inflammation in the tubes, the stroma, and the glomeruli, all the changes being most marked in the cortical portion of the kidney.

The epithelium of the convoluted tubes is often simply flattened. As this same appearance is also found in the chronic congestion of heart disease, it seems probable that the change in the shape of the cells is merely due to the inflammatory congestion.

In other cases, not only is the epithelium flattened but there is also a real dilatation of the cortex-tubes. This dilatation does not involve groups of tubes, but all the cortex-tubes uniformly. In other cases, the epithelium of the convoluted tubes is swollen, opaque, degenerated,

and detached from the tubes. But in fresh kidneys, properly preserved, this degeneration and desquamation of the epithelium is not nearly as constant or as marked a feature as would be supposed from the descriptions of some English observers. The tubes, whether with flattened epithelium or dilated, may be empty. More frequently, however, they contain coagulated matter in the form of irregular masses and of hyaline cylinders. The irregular masses are found principally in the convoluted tubes; they seem to be formed by a coagulation of substances contained in the exuded blood-plasma, and are not to be confounded with the hyaline globules so often found in normal convoluted tubes. The cylinders are more numerous in the straight tubes, but are also found in the convoluted tubes. They also are evidently formed of matter coagulated from the exuded blood-plasma, and are identical with the casts found in the urine. The tubes may also contain red and white blood-cells.

In the cases in which there is an excessive emigration of white blood-cells, we find these cells in the tubes, in the stroma, or distending the capillary veins. This excessive emigration is not necessarily attended with exudation of the blood-serum, and so the urine of these patients may contain no albumin. The white blood-cells are not usually found equally diffused through the kidneys, but are collected in foci in the cortex. These foci may be very minute, or may attain a considerable size.

In the glomeruli we find changes which, at first sight, seem peculiar, but are really similar to the changes which we find in arteries and capillaries in many inflamed tissues. The cavities of the capsules may contain coagulated matter and white and red blood-cells, just as do the tubes. The capsular epithelium may be swollen, sometimes so much so as to resemble the tubular epithelium, and this change is most marked in the capsular epithelium near the entrance of the tubes.

The most noticeable change, however, is in the capillary tufts of the glomeruli. These capillaries are normally covered on their outer surfaces by flat, nucleated cells, so that the tuft is not made up of naked capillaries, but each separate capillary throughout its entire length is covered over with these cells. There are also flat cells which line the inner surfaces of the capillaries, although not uniformly, as is the case in capillaries in other parts of the body. Still, in spite

of the presence of all these cells, the outlines of the walls of the capillaries are fairly distinct.

In exudative nephritis the swelling and growth of cells on and in the capillaries change the appearance of the glomeruli. They are larger, more opaque, the outlines of the main divisions of the tuft are visible, but those of the individual capillaries are lost. It is difficult to tell how much these changes in the glomeruli interfere with the passage of the blood through their capillaries. In most cases of exudative nephritis the patients recover and the glomeruli return to their natural condition.

In some examples of exudative nephritis we also find a thickening of the walls of the branches of the renal artery within the kidney. This thickening is principally due to a swelling of the muscle-cells in the walls of these vessels.

Etiology. Acute exudative nephritis is frequently a primary disease, either occurring after exposure to cold, or without discoverable cause. It complicates scarlatina, measles, diphtheria, typhoid fever, acute general tuberculosis, pneumonia, acute peritonitis, dysentery, erysipelas, diabetes, and many other of the infectious diseases and severe inflammations. It is one of the forms of nephritis which complicate the puerperal condition.

Symptoms. In the milder cases the only symptoms are the changes in the urine. This is somewhat diminished in quantity, of normal or high specific gravity; it contains albumin in moderate quantities, a few casts, sometimes blood.

In the more severe cases the changes in the urine are more decided. It is diminished in quantity, or even suppressed; its specific gravity is normal or high; the quantity of albumin is very large; the casts are numerous—hyaline, granular, containing white or red blood-cells or epithelium; there are also free white and red blood-cells and epithelial cells from the kidney and the bladder. As a rule, the quantity of albumin and the number of casts are in proportion to the severity of the nephritis, but this is not always the case. Large quantities of albumin, numerous casts, and many white and red blood-cells may be found in the urine of kidneys which after death show no structural changes; while, on the other hand, small quantities of albumin and a few hyaline casts are compatible with a severe nephritis. Still further, the number of casts found in the urine during life is not always in

proportion to the number of casts and quantity of coagulated matter found in the corresponding kidneys after death.

In addition to the changes in the quantity and composition of the urine, the patients present constitutional symptoms which vary, in the different cases, as to their number and their severity. A febrile movement, with more or less prostration; stupor, headache, sleeplessness, restlessness, muscular twitchings, and general convulsions; dyspnœa, loss of appetite, nausea, and vomiting; a pulse of high tension with exaggerated heart-action, or hypertrophy of the left ventricle; dropsy and anæmia—these may be called the characteristic symptoms of acute exudative nephritis. Of these symptoms a certain number—the fever, the prostration, the loss of appetite and nausea, the anæmia, the diminution in the quantity of urine, the albumin and casts in the urine—are such as would naturally accompany an acute inflammation of the kidney, and very often they are the only symptoms which do accompany it.

But with this same kidney lesion a certain number of patients will present, besides the symptoms just mentioned, the additional features of cerebral symptoms, changes in the heart and circulation, and dropsy. We, indeed, might think that the cerebral symptoms and the dropsy were due to the diminished excretion of urine; but when these conditions occur, as they often do, in patients who are passing large quantities of urine of good specific gravity; and when they are absent, as they often are in patients who are hardly passing any urine at all, it is evident that these symptoms are not directly due to the nephritis, but constitute a separate, complicating set of symptoms, which may be present or absent in any given case of the disease.

What the complicating lesion is which produces these symptoms we do not fully know; but the changes in the action of the heart and the dropsy, naturally direct our attention to the arteries and capillaries, with the expectation of finding in them some morbid condition which will hinder the passage of the blood through them. Whether the morbid condition is of an inflammatory nature, or whether it is only a spasmodic contraction, we are as yet ignorant.

The cases of exudative nephritis, with an excessive production of pus-cells, have a somewhat different clinical history. Such a nephritis occurs both in children and adults; it may be primary, or complicate scarlatina, diphtheria, or measles.

The *invasion* is sudden, with a high temperature and marked prostration. Restlessness, delirium, headache, and stupor are soon developed, and continue throughout the disease. The patients lose flesh and strength and pass into the typhoid state. Dropsy is slight, or absent altogether. The urine is not so much diminished in quantity as one would expect; its specific gravity is not changed—albumin, casts, and red and white blood-cells are present in considerable quantities, but not always early in the disease, and may even be absent altogether.

Prognosis. It is a very fatal form of nephritis, and yet one easily misunderstood on account of the resemblance of its symptoms to those of an acute meningitis.

Acute Productive or Diffuse Nephritis.—This is the most serious and important of all the forms of acute nephritis, not only for the reason that it involves so many of the structures of the kidney, but because its lesions are from the first of a permanent character, and because disturbances of the circulation are so frequently associated with it. It is one of the forms of scarlatinal nephritis, it occurs early and late in the course of diphtheria, it is the most important variety of the nephritis of pregnancy, and it is especially frequent as a primary nephritis with or without a history of exposure to cold.

Lesions. The changes in the kidneys are extensive and well marked. The kidneys are large, at first smooth, later sometimes a little roughened; the cortical portion is thick, white, or mottled with yellow or red, or congested; the pyramids are red.

In these kidneys we find the same lesions as have been described as belonging to exudative nephritis, but with two additional changes—changes which are found in the earliest stages of the inflammation and which give the characteristic stamp to the lesion: first, a growth of connective tissue in the stroma; second, a growth of the capsule-cells of the Malpighian bodies. Both these changes do not involve the whole of the kidney, but symmetrical strips or wedges in the cortex, which follow the line of the arteries. These wedges are small or large, few or numerous, regular or irregular, in the different kidneys. But in every wedge we find the same general characters: one or more arteries of which the walls are thickened; the Malpighian bodies belonging to this artery show an enormous growth of capsule-cells, with compression of the tufts; running parallel to these arteries

a growth of connective-tissue cells and basement substance in the stroma. Between the wedges we find at first only the changes of exudative nephritis, later a growth of diffuse connective tissue. Sometimes we find these wedges small, symmetrical, and at considerable distances from each other, more frequently they are much closer together, sometimes even becoming continuous.

If the nephritis is of acute type and recent, the new tissue between the tubes consists largely of cells; if the nephritis is of subacute type and longer duration, the tissue is denser and has more basement substance. Where the growth of new tissue is abundant, the tubes become small and atrophied.

In the wedges the constant change is the growth of new tissue in the stroma between the tubes, not an infiltration of the stroma with pus-cells, as in an exudative nephritis, but a new growth of cells and of basement substance. The tubes seem to become compressed and atrophied between the new tissue.

In each wedge is one or more of the arteries which run up into the cortex and give off the little branches ending in glomeruli. The walls of these arteries are thickened. The glomeruli belonging to these arteries become the seat of changes of a permanent character. There is the same growth of the cells covering the vessels, and of the cells within them, as in exudative nephritis, reaching even a greater development. In addition there is a growth of the cells lining the capsules to such a degree as to form a mass of cells compressing the tuft. The tuft, apparently, never returns again to its natural condition, but, as time goes on, the vessels are obliterated, the capsule-cells are changed into connective tissue, and the glomeruli are finally transformed into little balls of fibrous tissue.

Symptoms. The urine during the acute periods of the nephritis is scanty, colored by blood, of high specific gravity. It contains much albumin, numerous casts of all kinds, and red and white blood-cells. Exceptionally, the casts are few or absent. Later in the disease, or when it is of a more subacute type, the urine is more abundant, the specific gravity falls, the albumin and the casts continue. In the protracted cases, the albumin and casts may for a time diminish or even disappear.

The patients develop all the symptoms which we are accustomed to associate with Bright's disease — headache, restlessness, neuralgic

pains, delirium, stupor, coma, muscular twitchings, and general convulsions; dyspnœa and cough; loss of appetite, nausea and vomiting; neuro-retinitis; diarrhœa; increased arterial tension and hypertrophy of the left ventricle of the heart; anæmia, loss of flesh and strength; and dropsy, often developed to an extreme degree.

The course of the disease varies with the intensity with which it is developed, and the rapidity with which it proceeds.

The *invasion* may be sudden, the symptoms marked, and the duration of the disease short, with a fatal termination; or, with the same acute invasion, the disease may be protracted over many months, or the invasion may be gradual, the course of the disease subacute, the symptoms not continuous, but with periods of improvement or even apparent recovery, and the duration of the disease protracted for months and years.

The *prognosis* of this form of nephritis is bad. The lesion is a permanent and a progressive one. It is, indeed, apparently possible to recover from it, although with damaged kidneys, but this is the exception. The rule is that, sooner or later, the disease proves fatal, although it may well happen that periods of improvement give rise to false hopes of recovery.

Chronic Productive or Diffuse Nephritis with Exudation. —Although it is convenient to describe two forms of chronic nephritis, one with exudation and one without, yet it must be remembered that these are not separate lesions of the kidneys, but varieties of the same lesion. For in all these kidneys one form of inflammation—the productive, with the formation of new tissue—is present. The exudation from the vessels is something which is added to this, but does not change it.

In speaking of the exudation of serum from the vessels and its presence in the urine, we speak of it as it occurs during the whole course of the disease and not as it occurs for short periods. We mean that in an exudative chronic nephritis there is usually a large quantity of albumin in the urine, but that in the protracted cases there may be periods during which the albumin diminishes or entirely disappears. In the same way, in a non-exudative nephritis, there may be periods during which albumin is present in considerable quantities. Generally speaking, the character of the clinical symptoms will vary with the presence or absence of the albumin.

Lesions. In chronic nephritis with exudation the size of the kidneys is usually increased; there is a very extensive growth of connective tissue in the cortex; the renal epithelium is swollen, granular, degenerated, fatty, broken, or flattened; the tubes contain coagulated matter, cast matter, or blood; the cortex tubes are atrophied in some places, dilated in others.

The glomeruli are changed in several different ways:

1. There is a growth of the capsule-cells in such numbers that they compress the tufts. The cells covering the capillaries are also increased in size and number. The capsule-cells may finally be changed into connective tissue and the tufts become atrophied.

2. The glomeruli are of large size, the cells covering the capillaries are increased in number, so that the outlines of the capillaries are lost, but yet the capillaries are not compressed nor the glomeruli atrophied.

3. There is a growth of the cells which cover the capillaries and of the cells within them. Of the cells which cover the capillaries the cell bodies become very large, the capillaries are compressed, and the glomeruli eventually become atrophied.

4. The walls of the capillary vessels become the seat of waxy degeneration, while the cells which cover them are increased in size and number.

5. If the nephritis follows chronic congestion, the capillaries are dilated, and there is an increase in the size and number of the cells which cover the capillaries.

The arteries remain unchanged, or they are the seat of obliterating endarteritis, or there is a symmetrical thickening of all the coats of the artery, or all the coats of the artery are thickened and converted into a uniform mass of dense connective tissue, or there is waxy degeneration of the walls of the artery.

Causes. This form of nephritis occurs very frequently as a primary disease, especially in young adults. It follows acute diffuse nephritis, chronic congestion and chronic degeneration of the kidney. It may complicate syphilis, chronic phthisis, chronic endocarditis, prolonged suppuration, and chronic inflammation of the bone and joints.

Symptoms. The urine varies in quantity at different times. When the nephritis is most quiescent the quantity of urine is normal. During

the exacerbations of the nephritis the urine is scanty or suppressed. When the patients are doing badly, often when they are dropsical, the quantity of urine is very much increased.

The specific gravity and the proportion of urea to the ounce of urine slowly diminishes. In the cases of shorter duration the specific gravity is apt to run between 1012 and 1020. In the very chronic cases it will be between 1001 and 1005. Very low specific gravities regularly indicate a large growth of connective tissue in the stroma of the cortex, or waxy degeneration of the capillaries of the glomeruli.

The urine regularly contains albumin and casts. During the active periods of the disease the quantity of albumin is very large; during its quiescent periods it is smaller, and at times may entirely disappear. The number of casts varies in proportion to the quantity of albumin, but occasional exceptions to this rule are seen.

Dropsy may be considered a regular symptom of chronic exudative nephritis. It is rare to find a patient who goes through the disease without exhibiting this symptom. It may be developed at any time in the disease, continue uninterruptedly, or occur only in attacks. A peculiar pallor of the skin and a white color of the sclerotic are seldom absent, and are quite characteristic of the disease. They correspond to a diminution in the quantity of hæmoglobin and in the number of red blood-cells. These changes in the blood are not, as a rule, far advanced; but sometimes they are, and some cases even die with the symptoms of pernicious anæmia.

Many of the patients are troubled with headache and sleeplessness. Acute uræmic attacks, with contraction of the arteries, convulsions, etc., may occur in the course of a chronic exudative nephritis, but they are of very much more frequent occurrence with the non-exudative form of the disease.

Chronic uræmia, on the contrary, is one of the ordinary ways in which an exudative nephritis proves fatal. The patients pass into a condition of alternating delirium and stupor, with a rapid, feeble, soft pulse.

Simple neuro-retinitis, or nephritic retinitis are developed in a moderate number of cases.

Dyspnœa is a nearly constant symptom, but it is not always the same kind of dyspnœa, nor always produced by the same cause. It

may be due to hydrothorax, to œdema of the lungs, to contraction of the arteries, or to failure of the heart's action.

In many patients the dyspnœa due to contraction of the arteries, or to failure of the heart's action, is the first symptom which attracts attention. It is a dyspnœa which comes on in attacks, especially at night and in the early morning, and is regularly worse when the patient lies down. It often begins while the patient is apparently in good health, but it is a sure premonition of serious disease.

A catarrhal bronchitis with cough and expectoration is often present.

Loss of appetite, nausea, and vomiting, are frequent symptoms.

The heart is often affected. There may be hypertrophy of the left ventricle, dilatation of both ventricles, chronic endocarditis, myocarditis, or a feeble heart.

Course of the disease. There is hardly any limit to the variety of the disease, but the most constant symptoms are anæmia, dropsy, and albumin in the urine.

1. There are cases in which the symptoms are nearly continuous, the patients get steadily worse, and die within one or two years. The anæmia, the dropsy, and the albumin are constantly present, and the patients die with dropsy or with chronic uræmia.

2. There are cases in which the anæmia, the dropsy, and the dyspnœa come on in attacks which last for weeks or months. Between the attacks the patients are comparatively well, often able to work, although the urine always contains albumin.

3. There are cases in which a number of years before death the patient has an attack of dropsy, etc., from which he apparently recovers, and goes on able to work, but with urine of low specific gravity, which sometimes contains albumin. After an interval of many years comes the fatal attack with all the characteristic symptoms.

4. There are cases which for years have no symptoms but pallor of the skin and urine of low specific gravity containing albumin. These patients often for a long time feel so well that they cannot understand that they have a serious disease.

5. There are cases in which the first symptom is the attack of spasmodic dyspnœa, the patients otherwise feeling well. It may be months or years before the other symptoms are developed.

6. There may be a history of chronic endocarditis lasting for years before the renal symptoms are developed.

7. There are cases which apparently recover from the disease.

The *prognosis* is bad, but life may be prolonged for many years with but few symptoms, and recovery seems to be possible.

CHRONIC DIFFUSE NEPHRITIS WITHOUT EXUDATION.—*Lesions.* The larger number of these kidneys are found after death to be diminished in size; the two kidneys together may not weigh more than two ounces. The capsules are adherent, their surfaces are roughened or nodular, the cortex is thin and of red or gray color. A considerable number of the kidneys do not differ in their size or appearance from normal kidneys, except that the capsules are adherent and the surfaces of the kidneys are roughened.

Many examples of chronic non-exudative nephritis follow chronic congestion. The kidneys then remain hard, but the cortex becomes thinned, the capsules adherent, and the surface roughened. Some of the kidneys, instead of becoming atrophied, are increased in size, weighing together from sixteen to thirty-two ounces. The surfaces of these large kidneys may be smooth or nodular; the cortex is thickened, its color is red, gray, or white. There is regularly a growth of new connective tissue in the cortex and also in the pyramids, which becomes more and more marked as the disease goes on. In the cortex the new tissue follows the distribution of the normal subcapsular areas of connective tissue, is in the form of irregular masses, or is distributed diffusely between the tubes. In the pyramids the growth of new connective tissue is diffuse.

The tubes, both in the cortex and pyramids, undergo marked changes. Those included in the masses of connective tissue are diminished in size, their epithelium is flattened, some contain cast matter, many are obliterated. The tubes between the masses of new connective tissue are more or less dilated; their epithelium is flattened, cuboidal, swollen, degenerated, or fatty. The dilatation of the tubes may reach such a point as to form cysts of some size, which contain fluid, or coagulated matter. These cysts follow the lines of groups of tubes, or are situated near the capsules.

Of the glomeruli, a certain number remain of normal size, but with the tuft-cells swollen or multiplied. Many others are found in all stages of atrophy until they are converted into little fibrous balls. The atrophy seems to depend partly on the growth of tuft-cells and intra-capillary cells, partly on the thickening of the capsules, partly on the

occlusion of the arteries. If the chronic nephritis follows chronic congestion the glomeruli remain large, but with a marked growth of tuft-cells; or they become atrophied, but with the dilatation of the capillaries still evident. The capillaries of the glomeruli may be the seat of waxy degeneration.

The arteries exhibit the same changes as are found in chronic exudative nephritis.

Complicating lesions. Hypertrophy of the left ventricle of the heart is frequently caused by exudative nephritis, but still more frequently by the non-exudative form; but it must be admitted that such an hypertrophy, although frequent, is not constant, that both with exudative and non-exudative nephritis there may be no change in the wall of the left ventricle. The hypertrophy of the wall of the ventricle may after a time be succeeded by dilatation, a chronic degeneration, or myocarditis.

Chronic endocarditis is very frequently associated with chronic Bright's disease. The valvular lesions may cause chronic congestion, chronic degeneration, or chronic nephritis; or the same patient may suffer from chronic endocarditis and either form of chronic nephritis; the lesions are associated and possibly due to the same causes, but are not dependent on each other.

Pulmonary emphysema, chronic endarteritis, and cirrhosis of the liver, all of them examples of chronic productive inflammation, frequently accompany chronic nephritis.

With the endarteritis comes the additional danger of cerebral hemorrhage.

Patients suffering with chronic nephritis are more liable than are other persons to attacks of pericarditis, bronchitis, and gastric catarrh.

Symptoms. The typical urine of chronic non-exudative nephritis is a urine increased in quantity, of a specific gravity of about 1010, containing a diminished quantity of urea, without albumin or casts, or with a trace of albumin and a very few casts, except during exacerbations of the nephritis, when the quantity of albumin and the number of casts may be considerable. But very important modifications of the urine are of ordinary occurrence. It is quite possible, with nephritis of this type far advanced, to have urine not below 1020 in specific gravity, and without albumin or casts. In such cases the diagnosis has to be made without reference to the urine. On the

other hand, there are cases in which the specific gravity of the urine falls very low, almost to 1000, either with or without waxy degeneration of the vessels. There are cases in which the quantity of urine is very much increased, several quarts in the twenty-four hours. During the attacks of contraction of the arteries, to which these patients are liable, the urine may be diminished to a few ounces or suppressed.

In a great many of the cases cerebral symptoms are developed at some time in the course of the disease. Headache and sleeplessness are often present, the headache sometimes so severe and continuous that the patient is nearly maniacal; or instead of the headache there are neuralgic pains in the different parts of the body. Muscular twitchings and general convulsions are much more serious; they may be an early symptom, or not occur until late in the disease.

Hemiplegia with or without aphasia may be the first symptom to call attention to the nephritis, or may not occur until late in the disease. The invasion of the hemiplegia is sudden and is usually accompanied by coma. There is loss of motion alone, or of both motion and sensation. The hemiplegia, coma, and aphasia may continue up to the time of the patient's death, or disappear after a few hours or days. In the latter case the patient may have several attacks. These attacks have been ascribed to localized œdema of the brain. In the cases which I have seen there were no changes in the brain-tissue, but the cerebral arteries were damaged by chronic endarteritis.

Delirium, mild or violent, stupor, and coma may come on in sudden attacks, or be developed slowly and gradually.

When these cerebral symptoms come on in attacks, the arteries are contracted, the temperature is raised, and the patients are said to suffer from acute uræmia. Very often they recover from a number of these attacks. In the fatal attacks the pulse often loses its tension, but becomes rapid and feeble, and the patients die comatose with a feeble heart.

Instead of such acute attacks of cerebral symptoms, these symptoms may come on gradually in persons already much reduced by the kidney disease. The temperature is then apt to be below the normal, and the pulse is rapid and feeble.

Temporary blindness, neuro-retinitis, or nephritic retinitis, are developed in a moderate number of the patients.

Chronic bronchitis and emphysema very frequently exist, and the symptoms belonging to them often form a large part of the clinical history.

The left ventricle of the heart is regularly hypertrophied. This by itself gives no symptoms; but if the arteries become contracted, or if the hypertrophied heart becomes feeble, then disturbances of the circulation are established which cause serious symptoms.

In the same way, the complicating endocarditis which so often exists gives no trouble until the valves are a good deal changed, or the ventricles dilated, or the heart's action altered, or the arteries contracted; then the circulation is interfered with, and the results of venous congestion of different parts of the body show themselves.

Dyspnœa is a very frequent symptom, often the first symptom noticed by the patient. It is a spasmodic dyspnœa coming on in attacks which lasts for minutes, hours, or days. It is regularly made worse by mental or bodily exertion, or by the recumbent position. It does not resemble pulmonary asthma. It is apparently due to the association of changes in the arteries and in the heart. With contraction of the arteries alone, or with a feeble heart alone, no dyspnœa may exist. But if the contraction of the arteries is so great that the hypertrophied and laboring heart is unable to overcome the obstruction; or, if with the contracted arteries the heart becomes dilated or feeble, then the attacks of dyspnœa begin. At first the attacks are not severe and are of short duration, but if the mechanical conditions which cause them cannot be controlled they become longer and more distressing.

Perhaps the most striking examples of this dyspnœa are in the patients in whom it is the first symptom of the nephritis. They are apt to be middle-aged or elderly men, often engaged in large financial or commercial enterprises. They profess that they feel quite well and that they can attend to their affairs perfectly, but that they are very much annoyed because early every morning they have an attack of asthma. In spite of their professions of good health, it is evident that they are pale and that they have dyspnœa on exertion. The heart is found to be enlarged, with or without a murmur, its action either labored or feeble. The pulse is tense. The urine is of a

specific gravity of 1010 to 1030, it contains no albumin, or only a trace. In the earlier stages of the disease this dyspnœa can be controlled, but later on it is more distressing and difficult to remedy.

The stomach may become the seat of catarrhal gastritis, or of spasmodic vomiting. But in some patients it continues to perform its functions fairly well.

Dropsy, as a rule, is absent with non-exudative nephritis, unless it is complicated by chronic endocarditis, or cirrhosis of the liver.

Profuse bleeding from atrophied kidneys has been described by Bowlby in three cases.

Regularly, after a time the nephritis exerts its effect upon the nutrition of the patient, and the flesh and strength are diminished. On the other hand, the patients do not become as pale as they do in exudative nephritis.

Course of the disease. It is characteristic of the chronic productive inflammations of the lungs, the heart, the arteries, the liver, and the kidneys, that, while they often exist as serious and fatal diseases, they also frequently exist as lesions which do not interfere with general good health and long life. This seems to depend, in part at least, on the rapidity with which the inflammatory changes in these different parts of the body are developed. If they are developed slowly enough the functions of the organ continue to be performed in spite of the new growth of connective tissue in it.

So with the kidneys, it is common enough to find chronic non-exudative nephritis far advanced in persons who die from accident or intercurrent disease, and have never given symptoms of renal disease.

In the same way we can often observe for years persons who have urine of low specific gravity, an hypertrophied left ventricle of the heart, and occasionally some increase of tension in the arteries, and who yet habitually enjoy very fair health. But these same persons, if they are attacked with pneumonia, or pericarditis, or suffer from a severe accident, will often develop serious, or even fatal renal symptoms.

A very common form for the disease to take is that of attacks which are repeated a number of times, each attack worse than the preceding, and the general health more and more impaired between the attacks. During the attacks there are cerebral symptoms more or less severe—headache, sleeplessness, delirium, stupor, coma, convulsions. Dyspnœa

may be present or absent. The arteries are contracted, with a tense pulse. There is loss of appetite, nausea, and vomiting. The urine is of low specific gravity, and usually contains albumin. Between the attacks the patients at first seem to be fairly well, but later they gradually lose flesh and strength. The urine between the attacks is of low specific gravity and contains little or no albumin. They finally die in one of the attacks, or become feeble and emaciated.

In some of the patients spasmodic dyspnœa is the first symptom. This can often be controlled for months and years, and the patients then seem to be well. But after a time it is more difficult to manage, and other renal symptoms are added.

In some cases there are no symptoms for a long time, so that persons apparently in good health are attacked, without warning, by convulsions, coma, delirium, or hemiplegia. They may die in the first attacks or live to go through subsequent ones.

In some cases the only symptoms up to the time of the patient's death are gradual loss of flesh and strength and disturbance of digestion, the patient dying feeble and emaciated. These cases are hard to make out, unless the specific gravity of the urine is low and a little albumin present. Otherwise there is nothing to draw attention to the kidneys as the cause of the illness.

Loss of eyesight from nephritic neuro-retinitis may be the first symptom.

The patients may suffer from the symptoms of cardiac disease for years before the congestion or degeneration of the kidney is succeeded by chronic nephritis.

In many cases the course of the nephritis is modified by the complicating emphysema, phthisis, endocarditis, or cirrhosis of the liver.

Treatment.

Such a classification as this of kidney diseases brings with it a rational system of therapeutics.

Acute congestion of the kidneys can be relieved by the application of heat to the surface of the body.

Chronic congestion is best managed by the drugs which stimulate the heart and dilate the arteries.

We evidently have no means at our command by which we can influ-

ence acute degeneration of the renal epithelium; fortunately the great majority of the cases of acute degeneration are not serious.

Chronic degeneration also seems to be a condition which we are unable to treat.

In acute exudative and in acute diffuse nephritis the main indications for treatment are to diminish the severity of the nephritis and to regulate the circulation. To diminish the severity of the nephritis we employ cups over the lumbar region, heat over the lumbar region or over the entire body, and the internal use of calomel, sulphate of magnesia, opium, aconite, or digitalis.

The disturbances of the circulation are largely the causes of the cerebral symptoms and of the dropsy. With a laboring heart and contracted arteries we employ the drugs which dilate the arteries—chloral hydrate, opium, nitrite of amyl, and nitro-glycerin; or we diminish this quantity of the blood by venesection, sweating, or purging. With a feeble heart and relaxed arteries we use the cardiac stimulants.

In chronic nephritis, climate and mode of life constitute the important parts of the treatment; it is doubtful if drugs exert any effect on the nephritis. A warm, dry climate and an out-of-door life are of the greatest importance. Medical treatment can, however, be employed with advantage for the relief of the anæmia, the dropsy, and the disturbances of the circulation.

With the classifications of kidney disease now in common use you are all familiar. You know the number of names employed and the contradictory meanings attached to these names by different authors. Many of you must have experienced the extreme difficulty there has been in teaching students to understand Bright's disease. I leave it to you to determine how far the plan which I have proposed is likely to be of practical use.

DISCUSSION.

DR. ANDREW H. SMITH: With the discussion of Bright's disease the question of the significance of albuminuria is inseparably connected. But as preliminary to determining whether we have albumin in the urine we must decide as to what, or, rather, how much, shall be included in the term albumin.

Some studies which I have made recently seem to show that albumin, or, to be more precise, *serum-albumin*, is a very indefinite term; in fact, that it does not represent any definite chemical substance. Thus I find that a solution of Merck's "pure serum-albumin," in water, will give, when boiled, a precipitate. This being filtered out and the filtrate treated with nitric acid, a second precipitate is formed. Filtering again, and adding a strong solution of mercuric bichloride, we get a third precipitate. Filtering once more and agitating the filtrate with ether, a precipitate is formed which rises slowly to the surface. Finally, after filtering this out, agitation with chloroform throws down a dense, white, fifth precipitate.

Here, then, we have five distinct precipitates formed successively from the same portion of a solution of pure serum-albumin, and I have no reason to suppose that I have exhausted the possibilities in this direction. From these observations, coupled with the fact that chemists have never been able to fix upon a definite formula for albumin, no two specimens giving the same result on analysis, I think we are justified in the inference that there is no body having a definite chemical composition to which the name albumin can be affixed, but rather that, like the contents of a brewer's vat, it is a transition substance, the exact composition of which changes by insensible gradations as the transition advances, and that any given specimen is simply a mixture of different gradations, some of which respond to one test and some to another.

Now, clinically, what sort of precipitate shall be considered to decide whether a patient has or has not "albuminuria?" Shall it be the one obtained by heat, or the one by nitric acid, or the one by picric acid, or the one by Tanret's test, or the one by Millard's test, or the one by bichloride, or the one by ether, or the one by chloroform, or the one by some other "more delicate" test yet to be discovered? It is very important that this should be settled before we pass sentence upon a patient, particularly as at least two of the precipitates which I have obtained from serum-albumin can be obtained from the urine of every person in this hall. Normal urine agitated with ether will give a more or less abundant precipitate precisely similar to that from serum-albumin. Filtering this out and agitating the filtrate with chloroform we get a precipitate which again is precisely similar to that from serum-albumin. The inference which I draw from this is that under normal conditions there is an excess of nutritive material in the blood, and that a considerable share of the albuminous portion of this excess passes out through the kidneys, without having become at any time a part of the tissues. This overflow contains albuminoid material in various stages of elaboration, any stage of which may cause a response to some one test but not to others. There is no definite line of demarcation between those albuminoid substances which are normally present in the urine and those which are abnormal. The most we can say is that urine which responds to the coarser tests, such as heat and nitric acid, is more likely to be abnormal, while the more "delicate" tests may throw down normal as well as abnormal

constituents of the urine. Certainly ether and chloroform are tests so "delicate," that if their evidence were admitted all the world would have albuminuria.

DR. W. T. GAIRDNER, of Glasgow: I should like to say a few words on this subject because it is one in which I have long taken a great interest, although I have never seen my way clear to write a book about it. At a very early period in my career I had my attention particularly directed to the kidney. Somewhere in the later "forties" I was daily and hourly engaged in pathological investigations, which I need not say were very far short of those magnificent researches the results of which Dr. Delafield has just given us, but which nevertheless had the effect of fixing my mind early on this subject to such an extent that I have never been able, as a clinical teacher, to lose sight of the pathological department altogether since. While I shall not attempt to follow Dr. Delafield in the extremely important pathological points, I shall venture a few words from the point of view of the general physician.

First, let me say a word or two about names. Names are only symbols; still they are of great value and ought not to be dealt with loosely. Dr. Delafield seems to hint at this in the very title of his paper, where he speaks of "diseases of the kidney, popularly called Bright's disease." Are we justified in retaining this popular name, or not? On the face of it I do not like it—a disease called after a man. I do not think Dr. Bright himself would have wished or sanctioned the use of his name in connection with this disease. I do not know how you gentlemen feel about it, but, speaking for myself, I hope that if I go down to posterity at all, it will not be either in connection with a disease, or a pill, or a powder. I have a vivid recollection of the horror inspired by Dr. Gregory's name because of the preparation of rhubarb and lime bearing his name, which was the terror of our nursery. At the same time I think we must allow, all of us who have traced this subject historically, that there must have been something of practical expediency or necessity, felt as such at the time, in connecting Bright's name with this disease. Bright's own position in regard to this disease is a very remarkable one. He did not attempt to theorize about it at all. He stated facts. He very carefully guarded himself at all points in the statement of these facts, and if his followers since had been as attentive as Bright was to exclude all but carefully ascertained facts there would have been fewer of the faulty generalizations which have for a time pertained to this disease. What Bright said was: "There are some organic diseases of the kidney—*i. e.*, diseases attended by permanent changes of structure—which are associated with dropsy and with albumin in the urine, and the association of these facts is an important clinical indication which should be kept in view in diagnosis." Subsequently, in Guy's Hospital records, he developed almost all of what we now know—*e. g.*, the association of enlargement of the heart and certain alterations in the arterial system. All this can be found at least foreshadowed in his work. He did not name it Bright's disease. He did not approach a generalizing

theory of its pathology. He said that some of these different conditions which I have described may begin in inflammation. He did not say it was so; he said it might be so. All who have accepted these doctrines, and followed on Bright's lines, came to see that "Bright's disease" was a term which could not be dispensed with at that time.

Then we come to the book of Rayer, with its exhaustive historical summaries and its magnificent illustrations, a work which at once took hold of the French school in the same way that Bright's took hold of the English school. Rayer had no difficulty about generalizing and putting forth a theory, and he tried to cover the whole field of Bright's disease under the term "néphrite." He described first the "néphrite simple" and then "néphrite rheumatismale" (now daily recognizable as an embolic lesion), and then a long section of his work devoted to "néphrite albumineuse," in which he gives the most careful consideration to the whole subject. He covers all that Bright did before him (with very full acknowledgment, however), and tries to sweep it into a general category of a "néphrite." This had an unwholesome influence on the French school, by bringing in so broadly the idea of an inflammation as the elementary pathology of Bright's disease. At the time at which that book was written it led to bad practice—*i. e.*, the undue use of the so-called antiphlogistic remedies on the part of those people who acted upon these ideas. There was an impression created that Bright's disease, being an inflammation, must be treated as you would treat an inflammation in the arm or anywhere else—you must spare the kidney; you must, in case of dropsy, have the fear of inflammation of the kidney before your eyes, and you must, above all, omit the use of diuretics; that you might indeed use hydragogue cathartics, or otherwise act strongly on the bowels or the skin, but you must spare the kidney. There, again, was an imperfect or defective practice which followed on premature generalization.

It is perhaps useless to pursue the matter further as to its history. I only put this forward to show that the name Bright's disease, at the time it came to be so crystallized out, as it were, was practically the outcome of the necessary obscurity in which the pathology was left and of the unwillingness of Bright and great clinical physicians who followed him to be led into premature generalization.

The only other point which seems to require notice in the history of the subject since, is the threefold division given to it by Virchow. Virchow recognized that there were three types: The intra-tubular or parenchymatous nephritis—a disease of the epithelium which blocked the tubes and ultimately led to more or less permanent trouble; secondly, the inter-tubular or interstitial form; and lastly, there is the amyloid. This threefold division, with the great authority of Virchow behind it, has taken hold of the medical mind and has led my friend and colleague, Dr. Grainger Stewart, to speak of "Bright's diseases" instead of Bright's disease. Ever since then there has been a practical recognition of these three forms of renal disease as clinically and pathologically distinguishable—which is perfectly just; but I

rather think that the tendency has been too much to make these three forms absolutely distinct from each other and to overlook what I take to be probably the fact, that there must be an underlying unity, something common to all these three forms, when they lead to permanent disorganization of the kidney, which really marks out the thing as having the characteristics which lead us to the term Bright's disease.

Experience has taught me that the amyloid form is not, properly speaking, a form of Bright's disease. That seems rather an extreme statement. The amyloid form is accompanied by albuminuria; it is often fatal beyond all doubt; but it is fatal not because of the effects upon the kidney, but because it is an incident of other fatal diseases. That in itself would not perhaps serve to exclude it from the category of Bright's disease, but another point is that I believe the amyloid change is not necessarily a disorganizing change. I heard in Charing Cross Hospital, in London, an account of a case in which a man was admitted with extensive necrosis of bone accompanied with all the symptoms of amyloid kidney, amyloid liver, albuminuria, and every possible symptom of a constitution infected with amyloid disease. He had been considered in the first instance too ill to be operated upon. But nevertheless, a venturesome surgeon did it. He took off his leg. This patient had reached the last degree of exhaustion connected with amyloid supervening upon disease of his bones. The result, however, of the operation was a perfect return to the normal state. That singular case serves to show that there is nothing in the amyloid deposit itself which is, *per se*, destructive of the structure of the organs and which interferes with the kidneys returning to a healthy condition.

There is another form which is not included by Virchow—the fatty kidney. Dr. Delafield, however, dwelt on this subject. Fatty kidney *per se* is not Bright's disease. It is found apparently in domesticated animals; it is not associated with dropsy, not associated with enlarged heart, nor any of those symptoms found in Bright's disease. Bright's disease, even as a provisional name, ought not to be applied to anything that is not a permanent alteration of structure of the organ, therefore it is not, in my opinion, rightly applied to diseases of the kidney in which no other change exists than in the epithelium and in the occupation of the epithelial cells with a certain amount of oily granular matter. That fatty kidney is often associated with other changes which amount to Bright's disease, I very readily concede. We have now only two other classes—the intra-tubular and the extra-tubular or interstitial. But can we quite definitively separate these two classes? Admitting that there is a fairly broad clinical distinction which can be drawn between the extremes, can we separate these two classes in such a way as to justify our splitting up what we call Bright's disease into two departments? When the subject is investigated further I think we shall find something common to these two—something pathologically in common which really forms the essential change in a case of Bright's disease.

With respect to the last paper read, I cannot at all agree with the author.

I do not dispute his facts; but I cannot, as at present advised, admit that this substance, whatever it is (I do not presume to say what it is), which he gets out of the normal urine has any real pathological analogy with the albumin which is found in Bright's disease. I think this subject of the greatest practical importance in reference to insurance. I have been in the habit for many years of examining the urine of every case applying for insurance, and I have never pronounced the fate of a man upon any other test than those of nitric acid and heat. These tests are delicate enough for my purpose. But it is not a question of mere delicacy of the test, but of different substances and reactions. Albumin is not a normal substance, and I would most emphatically press home the fact that the appearance of albumin as obtained by the use of heat and nitric acid only is abnormal, and of the utmost importance in regard to insurance. I do not say that I would absolutely reject a man who has it, but I do say that from practical experience albumin revealed by heat and nitric acid, is a danger-signal, and ought to be pronounced as such and kept in view as such in every case.

DR. W. T. COUNCILMAN: I have been much interested in the paper of Dr. Delafield, because the subject of renal disease is one which has always interested me exceedingly, and I have made a careful study of all the cases which have been autopsied at the Johns Hopkins Hospital in the last two years, besides a number of other specimens. Dr. Delafield's proposition to classify the diseases of the kidney according to the nature of the morbid processes, and not according to the gross appearances of the diseased kidneys, is a very great advance. The chief difficulty arises in the great similarity of the pathological processes. For one thing, it is difficult to separate the degenerations of the kidney from the inflammations, for in every inflammation the primary lesion is a degeneration. Again, it is not certain that we can regard the exudation as the sole criterion of inflammation. I have tried to attack the subject in a general way from an etiological point of view. We must recognize that in every case of renal disease certain lesions are produced in the kidney. There are degenerations of the epithelium, fatty and hyaline, or simple atrophy, and in many cases associated with these, or more or less independent, lesions of the glomeruli and interstitial tissue. We recognize further that these lesions are in some cases focal, in others diffuse.

We might assume that so long as the kidney receives its blood-supply in normal amount, so long as that blood-supply is of a normal nature, so long as there is no change in the blood itself, and so long as the products of excretion of the kidney are not interfered with, so long as there is a ready way for their exit, that the tubes remain normal in the kidney for all time. In order to have change there must be some alteration in the character of the blood, or in the amount of blood which goes to the kidney, or in the pressure of blood, or there must be some interference with the removal of the excretion of the kidneys. Now, when we take into consideration the focal lesions of the kidney alone, we can recognize that these lesions are produced by injurious substances which reach the kidney in an insoluble form, or are due to a local

interference with the nutrition—that these are essentially the bacterial lesions of the kidney, or the lesions due to arterial disease of certain arteries. These insoluble substances in the blood are brought to the kidney and deposited in it in certain definite places, and there they exert their action, so that we can separate from other lesions the focal lesions produced by bacteria. These would be the various infectious lesions of the kidney, the tubercles, and so on, and abscesses. Then we must recognize another great class of cases in which the lesions are diffused, in which they are due to soluble substances brought to the kidney. Naturally, these substances being in solution in the blood will be distributed all over the kidney, and the lesions of the kidney, in consequence, will be diffused. These will be the lesions of the kidney which come on in consequence of all of the infectious diseases, and they will be the lesions, also, which will come on in consequence of chemical substances whose nature we do not very well know, and may constitute and do constitute a number of the varieties of the chronic diffused nephritis, or chronic diffused Bright's disease. We must recognize also that these injurious substances can reach the kidneys by other ways than by the bloodvessels. Of course, the only other way is by the ureters. We can have insoluble substances reaching the kidney by way of the ureters, and there producing certain changes in the kidney. We must recognize also that in the congestions of the kidney, if we carefully study fresh sections we can always recognize that in consequence of the congestions of the kidneys and the interference with the circulation of the kidney either by acute or chronic passive congestion, that certain degenerations are produced in the epithelium of the kidney in that way also. And then we can further recognize that there are certain lesions produced in the kidney by the result of the interference of the circulation by changes in the kidney alone; and just here will come in the very important changes in the kidney which always accompany the amyloid process. We do not know, so far as I am aware from the study of the kidney, any case in which we have amyloid change in the bloodvessel of the kidney pure and simple, without any interference with the nutrition of the kidney, without any degeneration at all, because these amyloid changes are almost essentially confined to the glomeruli—at least that is the point of the kidney which is almost always affected, and we know that all the blood of the circulation of the kidney passes through the glomeruli first, and if the glomeruli bloodvessels are amyloid, as they nearly always are, we have certain degenerative lesions in the epithelium of the kidney elsewhere which are directly in consequence of this. Now, too, we can have, as a result of all these lesions, conditions which will be very similar indeed. If these lesions act in a chronic way, if they are not very acute in their effects, and if they persist for a long time, we will have chronic lesions of the kidney. I think it possible that we can have almost the same macroscopic appearance of the kidney in a case in which circulation is interfered with, as in general endarteritis, and from long-continued action of some soluble morbific agent. In consequence of both of these processes changes are produced in the kidney, consisting essentially of degenerations,

followed by increase of connective tissue. We can have a granular contracted kidney in any of these conditions. Then, in acute lesions of the kidney in certain of the infectious diseases it is certain that in some cases some portions of the kidney are affected much more than others. Thus, in scarlatina and several other diseases the chief stress of the process falls on the blood-vessels of the glomeruli. In other cases the bloodvessels seem to be but very little injured, and yet we can have the most extensive lesions of the renal epithelium; we can have the most extensive fatty degeneration of the renal epithelium without any trouble in the glomeruli at all.

These are only some general points which have been suggested to me by the paper under discussion.

DR. VAUGHAN: I do not arise for the purpose of discussing the paper by Dr. Delafield; I should prefer to read the paper carefully before forming any opinion concerning the classification of diseases of the kidney which it proposes. I certainly think that Dr. Delafield is right in his objections to the further use of the term Bright's disease. There are diseases of the kidney which are different in their origin and in their pathology, and the fact that all of them have been grouped together under one name has, beyond doubt, produced an erroneous impression, even in medical minds, and has prevented advance in our knowledge concerning them. There is as much reason in grouping these various diseases of the kidney under one name as there would be for making the same disposal of all the structural diseases of the liver.

Dr. Smith has, I am sure, been led into error by the supposition that the preparation of Merck's serum-albumin, which he has employed, and which is labelled as chemically pure, is really pure. I have worked with the same preparation, and can say that it contains other proteids and inorganic salts. Alcohol will precipitate albumoses and peptones as well as serum-albumin. Ether precipitates egg-albumin, but does not precipitate serum-albumin. The precipitate with chloroform probably contains inorganic salts. In my opinion the three reliable tests for serum-albumin in the urine are: (1) the heat coagulation test; (2) the nitric acid test; and (3) the acetic acid and potassium ferrocyanide test. The precipitates with mercuric chloride, chloroform, etc., are not necessarily serum-albumin, and the employment of these tests is fallacious.

DR. A. H. SMITH: I wish to say that the only point I desire to make in this matter is, that in our striving after more delicate tests we are likely to run foul of substances which are normally in the urine. The moment you get away from the old tests of nitric acid and heat you are treading on dangerous ground.

As to this precipitate with chloroform being an emulsion: I have dried this at a temperature of 150°, and found in it a very solid residuum. I do not think the result of agitating chloroform with pure water can be for a moment confounded with the results which I obtained.

In regard to the impurities of Merck's serum-albumin, I have all along

maintained that it, or serum-albumin obtained in any form, is not a definite body, that it is composed of a number of things. But I can say at the same time, that exactly these reactions can be obtained with the white of egg, from which a good many of the substances which the gentleman before me has referred to can be excluded We do not have many of the constituents of urine in the white of egg. I simply claim that just as in a brewer's vat we have material which is passing from starch to sugar, and from sugar to alcohol, and in that mixture you can find starch and sugar and alcohol at any time, and that there is also a certain amount of material that will remain after all the starch and sugar and alcohol have been removed, which represents a transition going on: so there is a period of transition, I believe, going on in the blood, and I believe that the albumin of the blood is a transitional substance between the food and the ultimate tissue, that that transition develops a variety of stages, and that those stages respond to different tests. It seems to me, too, that the inference is justifiable that a good deal of nutritive material is taken into the blood and passed out of the kidneys without ever having been a portion of the tissue. The kidneys constitute a sort of overflow, as it were.

The material which is brought to the surface by ether is brought to the surface in large amount, and is albuminoid in character. It is not merely peptone. You can throw down the peptones with alcohol and still have these residues. It is a complex material which will not, all of it, respond to any one test, but portions will respond to one test and other portions to another. We are constantly liable, in our delicate tests, to confound albumin with something that is normally present in the urine.

RELATIONS BETWEEN ARTERIAL DISEASE AND VISCERAL CHANGES.

By GEORGE L. PEABODY, M.D.,
PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK.

THE subject upon which I have been designated to open a discussion this year by the Committee is so very comprehensive as to necessitate some limitation of an arbitrary character. As announced upon the programme, it might be held to include the results of atrophic changes in arteries, amyloid degeneration, hyaline degeneration, the various stages of atheroma, suppurating arteritis, embolism, thrombosis, and numerous other conditions, besides the one of chief importance, namely, *arterio-sclerosis*. It is to some few of the many important relations of the latter condition that I shall ask your attention.

Its nomenclature is still in a somewhat confused state, and about the more important circumstances of its etiological relation until recently there seemed no possibility of accord. At present, although a definite agreement has not been arrived at, there seems to be a tendency in such a direction.

An excellent and brief review of its early history is given by Orth in his *Handbuch d. spec. Path.*, Berlin, 1887, p. 229, where a good bibliography of the subject is also to be found.

The most generally accepted designation to-day—arterio-sclerosis—is the name given to it by Lobstein many years ago, and quoted by Virchow,[1] in 1856.

Rokitansky[2] called it simply an "auflagerungsprocess," and regarded the thickening in the arterial wall as caused by a deposit from the

[1] Ges. Abt, 1856, p. 498.

[2] Ueber Einige d. wichtigsten Krankheiten d. Arterien, quoted in Schmidt's Jahrsb. 1854, vol. lxxxi. p. 306.

arterial blood in consequence of some dyscrasia affecting that fluid. This position he subsequently surrendered, and accepted in its stead the theory that it was an inflammatory hypertrophy, in the formation of which some exudation from the adventitia might be concerned. This change of view was partly caused by proof which Risse[1] adduced, that the thickening in the vessel wall was covered by endothelium, which could not have been the case had it been due to a deposit.

The name given to it by Virchow in his classical writings upon the subject, was *Endarteritis deformans, s. nodosa*, writings all of which have still the ring of science and of truth, although improved methods and microscopes have tended to modify many of the views enunciated in them. He himself enumerates many of his contributions to this subject in a short controversial article in his own *Archiv* for 1879, vol. lxxvii. p. 380. Virchow held that the young cells which were found in recent growths of inflammatory tissue in the vessel-wall were to be traced to an inflammatory proliferation of the normal intima-cells. Traube, Köster, Talma, Cornil and Ranvier, and others, differed from him. Some were inclined to regard them as wandering leucocytes from the lumen of the affected artery itself, others as leucocytes from the vasa vasorum. Köster and his pupil Trompetter not only deny the cell-proliferation of the intima, maintained by Virchow, but claim that every endarteritis is dependent on a preëxisting meso- and peri-arteritis, and that the existence of all of these forms of vessel degeneration is wholly dependent upon the presence of vasa vasorum at the site of their formation.

Heubner (1874) regarded the process, as studied by him in the arteries of the brain, as being due to syphilis. Friedländer, in 1876, showed that this view was erroneous, that similar changes occurred in a great variety of conditions, that they were very widespread in the body and of great importance. He gave to the condition the name *arteritis obliterans*. Baumgarten,[2] three years later, also showed that from the *appearances of the growth in the intima alone* it was impossible to say whether the disease was due to syphilis or to one of many indifferent causes. He lays great stress upon the fact that in the appearances of the adjacent tissues may often be found charac-

[1] A. Risse: Observationes Quædam de Arteriarum Statu Normali atque Pathologico. Inaugural Dissertation, 1853.

[2] Virchow's Archiv, lxxvi., 1879, p. 268.

teristic evidence of syphilis. It is not likely to be limited to arteries of the brain, according to him, except in syphilis; but if you wish to be sure of this etiological factor in a given case you must look carefully for *other* evidences of it. Thus, it may occur in close proximity to a gumma; there may be masses of granulation tissue with caseous foci in the adjacent adventitia, and these may be in close relation to old diffused areas of fibrous peri-arteritis. All of these conditions would assist one in ascertaining the origin of a given arterio-sclerosis; but from the structure of the growth in the intima alone, it must be borne in mind that differential diagnosis is not possible.

Practically, the same is true of tuberculosis as a cause. If we find *other* evidences of tuberculosis, such as bacilli in the adventitia, a generalized process of tuberculosis, etc., the etiology of the case becomes simple; but from the location or appearance of the growth in the intima no such information can be obtained. In fact it is common enough to find in chronic phthisis near the pulmonary lesion well-marked arterio-sclerosis which is not of tubercular origin, but is to be regarded as a part of the cicatricial process which is induced by the tuberculosis.

Somewhat earlier than this, in England, Dr. George Johnson[1] showed that the walls of small arteries, in various parts of the body, were often greatly thickened in Bright's disease, and he ascribed the thickening chiefly to hypertrophy of the muscular fibres in their walls.

In 1872 Gull and Sutton read their famous paper before the Royal Medical and Chirurgical Society, in which they took the ground that the thickening in the arterial walls in Bright's disease was due to a hyaline fibroid formation, partly in the adventitia, partly in the intima. They found similar changes in the walls of the capillaries; they found generally an atrophic condition of the muscular layer of the arteries, while the inner and outer coats were thickened. It soon developed that the hyaline appearance was artificial, due to the action of the acidulated glycerin in which they had placed their preparations. Since the appearance of their paper in the *Medico-Chirurgical Transactions*, 1872, numerous other writers have described a hyaline degeneration of vessels. It seems likely that several different forms

[1] Med.-Chir. Transactions, 1868.

of degeneration have been described under this name, a change of this description occurring in different parts of the arterial walls under different circumstances. It is to be considered as rather an obscure and ill-defined condition in special pathology to-day,[1] whose causes and consequences need further investigation.

During the past fifteen years, since the writing of Friedländer just referred to, much attention has been devoted to this subject in different countries, and many papers have been published upon it, to some of the most important of which I shall ask your attention.

Probably the most important work upon this subject that has been done since Virchow's is that by Thoma, formerly of Heidelberg, now of Dorpat, published in Virchow's *Archiv*, vols. xciii., xcv., civ., cv., cvi., cxi., cxii., cxiii., and elsewhere. The latest publication from him with which I am familiar is a very brief review of his work on arteriosclerosis, in the *St. Petersburger med. Wochenschrift*, 1890, p. 360. It would be hardly feasible to present to you his arguments for the position that he maintains. His work impresses one as serious, painstaking, and ingenious, and his conclusions are of the utmost importance. We may not be able to accept them all, but in the main they seem to me to be entitled to very careful consideration. He tells us that while observers have long been agreed as to the extent to which this process is developed in the arteries, the cause of this fibrous growth in the intima has hitherto escaped detection. It had been observed as a common occurrence in arteries whose capillary system had been previously destroyed by ulceration, or by caseous or fibroid change. This had been so often seen that the conclusion had been reached that there must be some etiological relation between the disease in the artery and the change in its capillary system. But it was very doubtful which of the two conditions was the cause and which the effect of the other.

After carefully working over a kidney in which the process of interstitial inflammation was far advanced, one whose renal artery showed extensive new growth of the kind that we are studying, he concluded that *some change in the blood-current in an artery must result from an extensive destruction of its capillaries;* and, finally, by a very careful study of the aortic systems of nineteen bodies of

[1] Vide Ziegler: Path. Anat., 1890, vol. ii. p. 56.

fœtuses and young children, he reached further conclusions, which are of great interest. Even though it may seem to you, as it does to me, not quite safe as yet to accept all the conclusions to which he thinks his work has led, still a brief consideration of them will certainly repay us; and it may be well to begin with the kidney, and to say that he concludes that the interstitial inflammation in it is the cause and not the effect of the sclerotic process in the artery.

He finds that uniformly there develops a growth of connective tissue in the intima of the human aorta just after birth. This spreads throughout the entire arterial system which formed the direct communication between the ductus arteriosus and the umbilical arteries, at the same time that the intima of all the rest of the aortic system remains unchanged. What should cause this peculiar distribution of this growth? Is this arterial area subjected at the moment of birth to changed conditions which do not apply to the rest of the aortic system? It would seem so, and it would appear as if this newly formed connective tissue must be dependent upon some disturbance of the circulation consequent upon birth; and this, he thinks, can only be a *slowing of the blood-current in the aorta,* which is brought about by the closure of the two large arteries that cease to perform their function at birth, namely, the two umbilical arteries.

The physiological obliteration of these two large arteries and the loss of them as channels through which blood must be sent, causes the descending aorta to become suddenly disproportionately large—*i. e.*, too large for the due performance of its diminished function. The result must be, we are told, that the blood-current passes through it more slowly than it did in intra-uterine life. A careful review of the changed physiological conditions which occur in the aorta at birth and soon thereafter, would seem to justify this *à priori* conclusion, although it is not susceptible of demonstration. If this be so, then this part of the aorta must be diminished in size proportionately, if the circulation through it is to go on as before. The new growth of connective tissue in the intima, whose existence under these conditions is proved by the most elaborate and painstaking microscopic studies, tends to reduce the lumen of the aorta to the extent called for by the changed conditions. Not alone the existence of this new growth, which appears soon after birth, but its limitation to a definite region serves to prove that it is due to the cessation of the circulation in the

placenta. The fact of its restriction to that arterial trunk which leads from the ductus arteriosus to the umbilical arteries would seem to justify the conclusion that it is due to the disturbance of the relation in point of size between the descending aorta and its branches. In another paper[1] he shows that similar results follow in arteries whose capillary systems are suddenly diminished by surgical procedures, such as amputation, ligature, etc.

The so-called organization of the thrombus in arteries after ligature had been already shown by Baumgarten[2] and others to be really not an organization of the thrombus. The closure of the vessel after ligature had been shown to be due in part to a proliferation of connective-tissue cells from the endothelium of the intima, or from its deeper layers, in vessels whose intima is thick enough to have "deeper layers;" and in part to a mass of granulation tissue which comes from the adventitia, having found its way into the lumen of the vessel through the rent in the media, which always occurs at the site of application of the ligature. It is, therefore, a substitution of an organized tissue for the thrombus, rather than an organization of the thrombus, which takes place when the current of blood in an artery is suddenly checked by the application of a ligature; and the closure is partly effected by a process which is quite similar anatomically to that which we are studying.

To revert to Thoma's work. In all, Thoma has published eight papers on this subject, and numerous others on aneurism-formation and other allied topics. In the eighth paper[3] he gives a brief review of the most important points of his theory, and again designates this process "compensatory endarteritis," a name which he had previously given to it. He believes that the changes in the vessels come about in obedience to the following law: Every slowing of the blood-current in the arteries and veins of man, which is not completely and at once remedied by a proportionate contraction of the media, leads to a new growth of connective tissue in the intima which narrows the lumen of the affected vessel, and thus restores the normal swiftness of the blood-current more or less completely.

The empirical explanation of the changes in the vessel-wall advanced by Thoma is this: The lesion originates in the media, which

[1] Fortschritte d. Med., 1884, p. 713.
[2] Leipzig, 1877.
[3] Virchow's Archiv, 1888, vol. cxii. p. 10.

has lost its tone in some undescribed way. The defective elasticity of the media which results, allows a dilatation of the artery to take place, in consequence of which the blood-current flows more slowly than normal. This slowing of the blood-current produces a hyperæmia of the vasa vasorum and a new growth of connective tissue in the intima, with which there is associated later a similar formation in media and adventitia.

To go a little further back, the hypothesis would be that the sensitive nerve filaments in the arterial walls appreciate the change in the condition which surrounds them when the blood-current becomes slow, and, in consequence, they produce a reflex hyperæmia of the vasa vasorum. This functional disturbance of the vasa vasorum is the direct cause of the new growth of connective tissue, first in the intima, and then in the other two arterial coats. The tension of the arterial walls is the cause of the form taken by this growth in the intima.

As soon as the growth reaches such dimensions in any situation that normal rapidity of blood-current returns, the sensitive nerves are restored to their normal condition, the hyperæmia of the vasa vasorum ceases, and no more new tissue forms in the intima until the blood-current again undergoes changes of speed and again sets in operation the various factors in what might be called the causal nexus.

Thus, for Thoma, the explanation is purely a mechanical one; and though it has been more or less attacked, it seems to me to offer the best explanation of the cause and sequence of the phenomena that has yet been put forward. The distinction[1] which he draws between *primary* and *secondary* diffuse arterio-sclerosis is of importance. We have already noticed the importance which he attaches to the diminution in the resistance or resisting elasticity of the media as a factor in the etiology of the condition. In some cases the first recognizable departure from the normal consists in the stretching of this media (whose elasticity is less than it should be) by the blood-pressure, which need not be abnormally great. This is the cause of the diffuse primary arterio-sclerosis. This is characterized by a dilatation and tortuosity of the arteries, by an excentric hypertrophy of the media, and by a diffuse, conpensatory fibrous thickening of the intima.

[1] Vide Fortschritte d. Med , 1886, vol. iv. p. 496.

Thus to the dilated and somewhat misshaped lumen of the vessel a size suitable to the blood-current is supplied. From all of this there results a further diminution of the elasticity of the walls of the affected vessels which opposes an increased resistance to the blood-current, and thus becomes the cause of a secondary hypertrophy of the left ventricle, with the development of the *pulsus celer* as a symptom.

In other cases the diffuse arterio-sclerosis seems to depend upon more remote causes, which bring about disturbances of circulation in certain localized areas. Such,[1] for instance, would be a destruction or narrowing of smaller vessels derived from certain arterial trunks, by any pathological process. Thus it may be due not merely to a weakening of the contractile power of the elements that compose the media, but to an increased resistance in the periphery. In all such cases the rapidity of the blood-current is diminished in certain arteries. This is not regulated or removed by the contraction of the media, because this tunic has lost its elasticity. Thus all the conditions are present for the development of a compensatory fibrous thickening of the intima which will cause a diminution of the lumen, and thus give to it the size and shape which the new conditions call for. To these changes the name diffuse secondary arterio-sclerosis has been given. This also causes the same change in the heart and quality of the pulse as the other form. The increase in blood-pressure thus caused is sometimes followed by a slight degree of hypertrophy of the media.

Both the primary and the secondary forms of this affection are dependent for their origin upon a common factor, namely, a loss of mechanical contractile power or elasticity on the part of the media. Thus the two forms of this affection are often associated in the same person and become really only two subdivisions of a single disease, diffuse arterio-sclerosis. Where the masses in the intima are circumscribed,[2] forming the arterio-sclerosis nodosa, the cause is the same as in the primary form just described—*i. e.*, a slowly developing loss of elasticity and consequent yielding of the media. This causes a slowing of the blood-current, with the consequences so often dwelt upon. The stretching of the arterial wall takes place gradually, and *pari passu* the growth of connective tissue occurs in the intima. This

[1] Welch: Maryland Med. Journal, 1891, p. 76.

[2] Virchow's Archiv, Bd. cv. pp. 1, 11. Also Fortschritte d. Med., 1886, Bd. iv. p. 563.

being the case the deeper layers of the *newly formed* connective tissue must also be subjected to the stretching process as other layers are formed upon them. A consequence of this stretching is the development of degenerative changes in these outer layers of newly formed connective tissue, those lying next to the media. Among the forms of degeneration to which this tissue is liable are calcification, fatty, hyaline, and atheromatous changes. These degenerative changes seem to be characteristic of arterio-sclerosis nodosa. In some cases serious changes like these are negatived by a further compensatory formation of connective tissue in the intima over them. The points of origin of arterial branches[1] seem to be favorite sites for the development of the nodose form. Thus there develop at these sites various circumscribed deformities of the lumina of vessels.

The hyaline and atheromatous degeneration in the new tissue are marked by a more or less distinct swelling, which often causes the compensatory thickenings of the intima to project somewhat into the lumen of the vessel, and thus to interfere with the blood-current, and also to narrow the lumen of arterial branches at their sites of origin in the mother vessel. Various and grave disturbances of nutrition may, of course, result in the organ to which these branches go, and it is conceivable that often thus a vicious circle is established. Thus the diseased arteries supply less blood to a given organ than its proper nutrition requires. Local degenerations ensue in the organ. These changed conditions call for still less blood, and there results a further disturbance in the rapidity of the current in the nutrient artery. This causes further changes in the vessel's intima.

I have purposely omitted histological details, inasmuch as I felt sure that they would be so much more ably dealt with by my colleague.

Pekelharing,[2] in a recent paper, accepts Thoma's main conclusions, but endeavors to explain the cause of the proliferation of the endothelial cells from the inner surface of the intima, by supposing an alteration in blood-pressure in the interior of the diseased vessels. By some carefully devised experiments he seems to show that if the blood-pressure be diminished the intima grows. His idea is that under ordinary circumstances the pressure exerted on the intima by the blood is sufficient to prevent any growth except such as may be needed for

[1] Virchow's Archiv, Bd. cvi. p. 111. Also Fortschritte d. Med., 1887, Bd. v. p. 70.

[2] Beiträge zur path. Anat. und zur allg. Path., Jena, 1890, vii. p. 245.

repair, but that if the pressure be diminished, then the endothelium can grow in excess of the needs of the system until a normal pressure be again exerted upon it.

How are we to account for the alteration in the rapidity of the blood-current, if that be the initial local factor in the series of events which leads to the development of the arterial changes under consideration? To this question the answer is vague and unsatisfactory. The change in the rapidity of current is not susceptible of proof. We are to infer its existence from the facts which have been already adduced. When we endeavor to explain its cause we begin to deal in generalities, which are unsatisfactory to the seeker after the exact. Its cause[1] is to be regarded as a general disturbance of nutrition, which may be due to infections of various kinds, or to different kinds of pathological processes or to senile changes. These general disturbances of nutrition cause disease not only of the arteries, but of the veins and capillaries as well.

Arterio-sclerosis can occur in a great variety of conditions. Unless we accept Thoma's conclusion, it is still often difficult to determine whether it is the cause or the effect of the morbid process by which it is accompanied. It is a common occurrence in inflammations in which the formation of connective tissue is at all a prominent factor. Thus it is often seen in connection with cirrhotic changes in the kidney, in the testicle, in chronic inflammatory processes of lungs, of Fallopian tubes, in many neoplasms, especially those accompanied by abundant connective-tissue formation, such as elephantiasis, fibroma, carcinoma, epithelioma. Heredity, syphilis, gout, rheumatism, old age, chronic alcoholism, all seem to be important etiological factors in the development of this arterial change, and to these Thoma has added functional arterial strain.

Sack[2] has studied the topographical distribution of the disease throughout the arterial system. He finds that, physiologically, there exists in the common carotid a subendothelial layer of connective tissue, which increases steadily in thickness, and never becomes very thick. If diffuse arterio-sclerosis be present, this growth in the carotid increases very materially in thickness. The explanation of this con-

[1] St. Petersburger med. Wochenschrift, 1890, No. 40, p. 360.

[2] Sack: Virchow's Archiv, 1888, cxii. p. 403.

dition of things in the carotid is this: This artery has attained almost its complete development by the tenth or twelfth year. As the rest of the arterial system grows after that, and accommodates more blood, the carotid is subjected to frequent or even constant stretching. After a time this over-stretching causes it to lose much of its elasticity, it becomes unable to return to a proper size, and becomes too large for the amount of blood that it has to transmit. Under these circumstances it is easy to account for a compensatory sclerosis. Sack's results in the matter of topographical distribution of this disease show a difference between the diffuse and the nodose form. The former selects the arteries of the extremities, the latter the aorta and carotid. The arteries of the extremities are subjected to more hydrostatic pressure than those of the interior of the body, by reason of their remoteness from the heart, and hence they are more likely to be diffusely dilated, and to need the compensatory sclerosis in consequence. The nodose form depends, however, upon local weakness or disease of the media; and it is in the aorta and carotid that the force of the heart's action is likely to cause such localized stretching, especially by reason of the branching and change of direction to be found in them.

Sack gives a scale showing frequency of occurrence of sclerosis of all forms and grades in different arteries, with 100 as a maximum. The following is the order of frequency:

Tibialis anticus	94
Ulnar	92
Radial	79
Popliteal	72
Femoral	64
Ascending aorta	58
Common carotid	58
External iliac	53
Abdominal aorta	52
Brachial	51

When it occurs as a degeneration of old age it has a great variety of locations. Its development may be very slow, and it may chiefly affect the aorta; it may be confined to the arteries of a single organ, or it may extend to those of several organs, or it may be found in many or in most of the organs.

If none of the recognized causes exist and still the lesion occur, then

we are inclined to ascribe it to tobacco or lead, or to some of the exigencies of life (not more nearly defined) to which the patient has been exposed. Of late, too, endocarditis, typhoid fever, and scarlet fever, have been included among the remote causes of the lesion. If it occur in the vasa vasorum, it may be the cause of a localized atheroma, this degenerative process following upon the interference with the blood-supply to the vessel's wall.

Let us consider now some of the more important effects of these changes in the arteries.

Of late years much has been written on the subject of the relation of arterio-sclerosis to aneurism;[1] and although all agree that the two conditions often occur together, there seems to be no little discrepancy with regard to their relations from an etiological point of view. It may be interesting to devote a few moments to this matter, with the premise that it is not claimed by anyone that arterio-sclerosis is the sole cause of aneurism.

It it susceptible of experimental proof[2] that in the early stages of the affection the arterial walls are weakened and dilatable. The walls are still elastic, but less elastic than normal, so that if the pressure within be gradually increased the lumen is increased to a much greater extent than is the case with a normal artery under similar circumstances. In the next stage, the thick layer of connective tissue in the intima renders the vessel fully able to withstand momentary increments of pressure from within. It seems probable, therefore, that the arterio-sclerotic aneurism develops during the first stage of arterio-sclerosis. Thoma tells us that at this time the wall of the artery is so far weakened that it is perfectly easy to produce artificial aneurisms in the vessel removed from the body during life or after death by a pressure of from 12 to 24 centimetres of mercury. This cannot be done either with normal arteries or with such as present an advanced degree of arterio-sclerosis.

It is of interest to know that the early stage of this lesion, the time when the arteries are easily dilatable, is supposed to last only a year. As a result of experiment and calculation the inference has been drawn that a year after the beginning of the disease in a vessel, the

[1] Thoma: "Untersuchungen über Aneurisma." Five papers, Virchow's Archiv, Bd. cxi.–cxiii.; Deutsche med. Wochenschrift, 1889, xv. pp. 340, 361.

[2] Deutsche med. Wochenschrift, 1889, p. 341; also Virchow's Archiv, 1889, cxvi. 1.

intima is to such an extent reinforced by newly-formed connective tissue that liability to formation of aneurism may be excluded. It should be remarked that this period of time applies, not to the whole arterial system (in Thoma's calculations), but to each diseased vessel—that is to say, the various arteries may become diseased in succession throughout the body; and from the beginning of the development of weakness in the muscular coat in the case of each vessel, a year must be allowed to elapse before liability to aneurism in that particular artery has passed. "Every individual who is the subject of arterio-sclerosis is thus for a year exposed to the danger of aneurism in all parts of his arterial system. This period occurs chiefly between the ages of thirty-five and forty-five years." *We* should probably want stronger evidence of the truth of such exact inferences than seems to be forthcoming before we accepted them.

It is of great clinical interest that this weakness of the arterial wall which marks[1] the early stages of arterio-sclerosis can be diagnosticated by ophthalmoscopic examination. The evidences of its presence are said to be tortuosity of the arteries, pulsation and locomotion visible in them (without other explanation, such as chlorosis, anæmia, neurasthenia), opacities in their walls, often a diminished lumen, hyaline degeneration of some vessels of papilla, occasionally aneurism of the central artery, and oftener varicose veins. Complete obliteration of an artery has been seen, and thickening of the walls of veins with partial obliteration of their lumina. It is altogether likely that changes like these in the central artery of the retina, and in the ophthalmic artery, are associated with changes in the internal carotid. It is believed that the rest of the arterial system may be intact and yet serious changes show themselves in the carotid and its branches.

Of ninety cases of arterio-sclerosis examined by Raelhmann, forty-four showed lesions in the fundus of the eye. The same writer elsewhere[2] records a case of sudden total blindness in a puerperal woman after severe bleeding, whose death occurred eight weeks later from a second uterine hemorrhage. Autopsy showed the cause of the blindness to be a condition of arterio-sclerosis with local narrowing of

[1] Thoma: Deutsche med. Wochenschrift, 1889, No. 18, p. 362; and Archiv für Ophthalmoscopie, 1889, xxv.; Raehlmann: Zeitsch. für klin. Med., 1889, xvi. 506.

[2] Fortschritte d. Med., 1889, vii. p. 928.

the lumen in many places and consecutive retinal œdema. Much of Raelhmann's work is confirmed by Goldzieher[1] in a recent paper.

These observations have more recently been confirmed and added to by a French writer.[2] He has seen hemorrhages in retina, in choroid, in optic nerve and its enveloping membranes, as well as miliary aneurisms, besides the arterial changes just mentioned. These are regarded as important diagnostic signs of the initial stage of arterio-sclerosis. Inasmuch as liability to aneurism and laceration of arteries is greatest at this time, it would seem logical to warn patients who manifested these symptoms from exposing themselves to exciting causes which are known temporarily to increase arterial tension. It is calculated that the critical period is about the fortieth year, as we have seen; and that if, with these early signs of arterial change, men will lead circumspect lives for a few years at this time, they may escape the danger of arterio-sclerotic aneurism until the liability is passed, or until the compensatory sclerosis has taken place. There seems to be experimental proof of much of this. In dogs arterio-sclerosis rarely occurs spontaneously. If the aortic valve is lacerated, the sphygmograph at once shows in the femoral artery all the usual indications of aortic insufficiency; in the next few days no changes are observable in the arterial system; a few days later tortuosity and pulsation of the retinal arteries become visible, and at this time examination of pieces of arterial trunks removed from the body shows that they have become defective in point of elasticity, and that they can be dilated more easily than normal arteries. After the lapse of two or three years, the tortuosity of the retinal arteries persists and a diffuse arterio-sclerosis can be distinctly made out by microscopic examination. The use of the sphygmograph and the importance of an accentuated second aortic sound in diagnosticating the increased arterial tension which is often characteristic of the early stages of these changes are both well recognized.

The relation of the sclerotic process to the formation of aneurism is thus conservative, although the antecedent stage of weakness of the media would seem to be a predisposing cause of that grave disease.

We have seen that arterio-sclerosis is a common cause of left ven-

[1] Centralblatt für prakt. Augenh., Leipzig, 1889, xiii. p. 361.

[2] Koenig: "De l'Artério-sclérose et des Affections Oculaires que en Dependent." Thèse, Paris, 1890.

tricular hypertrophy; and yet it is a common experience for every pathological anatomist to find a small, atrophic, pigmented heart when this arterial lesion is combined with aneurism. This has recently been explained by Högerstedt,[1] after the narration of such a case. The way in which arterio-sclerosis causes hypertrophy is by overtaxing the muscular force of the heart by increasing the resistance to be overcome; this occurs in consequence of a diminution of the elasticity of the arterial system. If now an aneurism exist early in the process (and it is not likely to occur late), this lack of elasticity is in part thus compensated and the aneurism aids somewhat in the propulsion of the blood through the diseased arteries. The inference is that the aneurism acts to replace the partially lost elasticity of the arteries, much in the same way that the rubber bulb contributes by its elasticity to the generation of a continuous current in the ordinary hand-atomizer.

If the vascular lesion be once well pronounced it becomes capable of causing grave secondary changes in the region supplied by the affected vessels, as has already been stated.

The combination of a syphilitic endarteritis with a peri-arteritis has often been the direct cause of cerebral softening; and in other cases has caused a thrombus to form at its site with the same result so far as the nutrition of the brain is concerned. Cases of this kind have repeatedly come under my observation and been followed to the post-mortem table. Softening of the brain from diffuse arterio-sclerosis has often occurred without the causative influence of syphilis. Such a cause was reported by Ball and Seguin[2] several years ago.

It has occurred very early in life as a lesion of syphilis. In a syphilitic child of twenty months it proved fatal after characteristic disturbances of cerebral function. No autopsy was permitted in this case, which is published by Seibert,[3] but the diagnosis seems to have been carefully made. Leudet[4] records an interesting case of recovery from what he considers to have been syphilitic arteritis. His patient was a man, fifty-three years old; he had the usual "head symptoms,"

[1] St. Petersburger med. Wochenschrift, 1889, xiv. 18, 19.

[2] Archives of Medicine, New York, 1881, vol. v. p. 136.

[3] N. Y. Jahrb. d. Kinderheilk., 1885, xxii., 4, p. 333; quoted in Schmidt's Jahrb., vol. ccvii. p. 266.

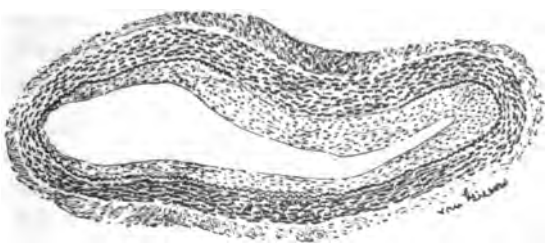
[4] L'Union Méd., 1884, 146; quoted in Schmidt's Jahrb., vol. ccvii. p. 265.

with which we are all familiar, syphilitic infection having occurred four years previously; but in addition to these symptoms he manifested others of unusual occurrence—*i. e.*, he suffered from lancinating pains in the scalp in the neighborhood of branches of the temporal arteries; these vessels gradually became stiff, hard, and swollen. All symptoms gradually disappeared after four months of specific treatment. Here the lesion occurred in superficial arteries coincidently with its occurrence in those of the brain; and its cure was brought about in both sets of vessels by ordinary specific treatment.

It seems occasionally to cause death in early life by cerebral hemorrhage. It is probable that aneurism-formation is the immediate cause of the rupture of arteries, in young subjects as in old, when it occurs early in arterio-sclerosis.

Some years ago a boy, nineteen years of age, died of cerebral hemorrhage in the New York Hospital, in whose arteries this lesion was very distinct (Fig. 1). I have the pleasure of showing you a few

FIG. 1.



Internal carotid artery of a boy nineteen years of age, who died of cerebral hemorrhage. It shows the lesion of arterio-sclerosis.

sections of one of his internal carotid arteries in which the sclerotic process is well seen.

W. J. F. was a canvasser by occupation. He was said to have been in good health prior to this illness. Unfortunately his history is meagre. He was known to be well at 1.30 A.M. on December 4, 1884. Two hours later he was found comatose and was brought immediately into the hospital. Fifty minutes after he was found in this condition he died, having remained absolutely comatose all the time. The autopsy, which I made several hours later, showed very extensive cerebral hemorrhage with great laceration of brain; and, beside this, it showed arterio-sclerosis very generally throughout the body. I have records of the presence of this lesion in both internal

carotids, one common carotid, both renal arteries, and the small arteries in the substance of both kidneys. The aorta was very small, measuring in diameter at the beginning of the transverse portion of the arch 1.6 cm.; at its bifurcation 1 cm. There was distinct hypertrophy of the left ventricle, and the kidneys were atrophied, and showed by microscopic examination the lesions of chronic diffuse nephritis.

Virchow[1] has called attention to the fact that in cases of congenitally small aorta, like this one, there seems to be a tendency toward the development of degenerative changes in the intima, such as sclerosis and atheroma; and occasionally, also, fatty changes in the media and myocardium. He also speaks of hypertrophy of the left ventricle as occurring in this condition. I regret that at that time I was not specially interested in this subject; hence my investigation of this case, both clinically and anatomically, must appear to you very unsatisfactory.

It would be easy to adduce many cases of death from this disease in the cerebral vessels occurring in middle life; but it would perhaps not be profitable to do so. It is sufficient to say that it is common; that it is often of syphilitic origin; that it is then usually accompanied by definite symptoms of which pain is a marked one; that it is likely to be associated with peri-arteritis; that it disturbs brain-function by depriving specific areas of their blood-supply; that it may do this with or without an accompanying process of thrombosis; that it is, when due to syphilis, very amenable to treatment, if the treatment be sufficiently early and sufficiently energetic; that if it be not properly treated it is likely to lead to death by cerebral softening.

All of this is commonplace. Less so is the question as to whether death can be caused by this lesion preceded by symptoms of disturbance of brain-function, such as hemiplegia, aphasia, etc., *without* lesion of the brain. I believe that it can, that it has occurred in my own practice. The following case,[2] published elsewhere some years ago, seems to illustrate this possibility:

J. M., aged fifty-six, a native of Ireland; widower; a tailor by occupation; was admitted to my service in the New York Hospital, April 22, 1886. He gave the following history: His mother was rheumatic; of his father he

[1] Ueber Chlorose u. die damit zusammenhängenden Anomalien im Gefässapparate, u. s. w. Berlin: A. Hirschwald, 1872. Also, Schmidt's Jahrb., 1872, Bd. clvi. p. 339.

[2] N. Y. Medical Record, 1886, p. 65.

knew but little. He said that he (the patient) had had rheumatism in his hips for six years. He denied malarial history. He had a soft chancre years ago, and suppurating bubo, but he denied symptoms of syphilis. He had partaken immoderately of spirits for the past twelve years. During the entire past winter he had suffered from a continuous headache and from ringing in the ears; he had not been dizzy. About ten days ago he fell suddenly to the floor and was unable to move either of his right extremities, and was unable to talk. He did not lose consciousness. In half an hour he was able to talk, and power had returned in great measure to his leg, but less completely to his arm. Recovery, however, was ultimately complete. Four or five times since then he had had slighter attacks of a similar character, when he could not speak or move, but recovered always in a few minutes. There was never any loss of consciousness. He never had an attack before ten days ago. His appetite was fair, his bowels regular; his temperature is 100.6°, respiration 24, and pulse 82, on his admission to the hospital at 11 A.M. He was senile; his superficial arteries were stiffened and tortuous; he was poorly nourished; there was no œdema; there was incomplete right facial paralysis; the tongue, on being protruded, deviated to the right; there was well-marked right hemiparesis; there was no disturbance of sensation.

There was lateral curvature of the spine; the chest was barrel-shaped; the heart-sounds were normal.

His urine gave the following results on examination: Reddish-yellow, acid, 1.024, no albumin, negative microscopically.

Treatment: Potass. iodid., grs. XX, every three hours.

April 23—3 A.M. He had a seizure at this time, characterized by loud, gasping, stertorous breathing, and complete inability to speak or protrude his tongue; his pupils were normal; he could move both arms and legs, but there was marked diminution in the power of both of his right extremities; consciousness was complete. In about half an hour he recovered from this attack, was able to speak perfectly, and told accurately all that had happened. He could protrude his tongue readily, it deviated somewhat to the right; his temperature and pulse were normal; his respiration somewhat accelerated. The iodide of potassium was increased to grs. XXX at a dose. He felt well, and was allowed solid food at his own request. In the absence of the attendant he tried to get into bed from the night-stool this morning, but fell, and was unable to get up without assistance. At 5.30 P.M. he had an attack similar to the previous one; it lasted forty minutes; recovery from it was slower and less complete. He could soon protrude his tongue, but with difficulty; he could talk so as to be understood, but talking was difficult, and his speech was indistinct.

24*th*. During the early part of the night he again got out of bed and fell, and was quite restless. He said that after both attacks his head ached very severely, and he was unable to eat. Very early this morning he had a similar attack, but much more severe than any of the previous ones; at 4.30 A.M. he was still suffering from it, was conscious, but now was entirely unable

to move the right side. At 9 A.M. he was unconscious, in a profuse perspiration, and breathing with marked stertor; his temperature was 104° F.; respirations 52; pulse 129. He continued in this state, rapidly growing weaker, until 1.45 P.M., when he died. The temperature after death was 105.8° F.

The autopsy was made about an hour after death. The weather was warm, and, therefore, to prevent the occurrence of post-mortem changes, the body was taken directly from the ward to the autopsy-room. It was fairly nourished; rigor mortis was absent; there was no œdema; the organs generally were normal; the cortices of the kidneys were a trifle thin, but the surfaces were smooth and the markings distinct; there was slight hypertrophy of the left cardiac ventricle; there was a mass of grayish-yellow material in the liver, measuring two by three centimetres, it contained caseous material, and proved on examination to be surrounded by a layer of connective tissue, and to be an old gumma.

With the exception of the brain, now to be described, the other organs were substantially normal.

The arteries in the circle of Willis showed several small, insignificant patches of atheroma; in most of them, notably the basilar and left middle cerebral, there was a well-marked growth of connective tissue in the wall of the intima; the calibre of the vessels was thus distinctly encroached upon, but by no means completely obliterated; in many of these regions was found the small-celled growth of peri-arteritis as well. There was no alteration in the color or consistency of any part of the brain, and no other change was found.

A microscopic examination of the affected arteries showed the lesion to be arterio-sclerosis, which involved to a varying degree almost the entire circumference of the vessel. The lumen was thus not obliterated, but very materially encroached upon.

The possibility of the occurrence of death under such circumstances, with brain-symptoms but without brain-lesion, is alluded to by Delafield and Prudden;[1] but I have not found any recorded cases. The explanation of the cause of death here is not entirely clear. It seemed to me that there might perhaps have been a spasmodic contraction of the muscular coat of the middle cerebral artery, or of several of its branches; which, in addition to the encroachment upon its lumen, produced by the new growth, was sufficient to cut off blood-supply to the parts to which it was distributed; that this had occurred several times, causing each time temporary ischæmia of important brain centres; and that in the final attack it had lasted long enough

[1] Handbook of Path. Anat. and Hist., New York, 1889, 3d ed., p. 290.

to produce death, but that it was not complete enough, or of long enough duration, to cause softening.

That similar arterial spasm takes place in the retina,[1] and can be seen with the ophthalmoscope, there seems to be abundant evidence; that it occurs in the coronary arteries seems extremely likely, from the occurrence of sudden death from cessation of heart-action without embolic or other permanent closure of a sclerosed coronary artery. I have myself diligently sought to find other cause of sudden death in a subject of angina pectoris, whose heart-muscle was not degenerate, and believe that arterial spasm alone will account for it under these circumstances.

The effect of this disease, occurring in the coronary arteries, has been very carefully studied, and many contributions have been made to the literature of this part of the subject.

Independently of the serious effects produced in this way, there seems to be good ground to believe that valve-lesions, especially of the aortic valve,[2] are often caused by changes in the small arteries which supply them.

That angina pectoris should be produced by this lesion in the coronary arteries needs only to be mentioned. In passing it may be proper to say, however, that this is not the only cause of that serious and painful disease.

That arterial spasm, localized and general, seems to be brought about by this lesion, as already remarked, seems again proved by the fact that attacks of angina often are accompanied by differences in radial pulses,[3] by localized areas of anæmia, and by increased arterial tension in general.

Sudden transitory blindness is known to occur in one or both eyes in conditions of aortic stenosis, and the explanation offered for it is spasm of the cerebral arteries.[4] It is known that in generalized arterio-sclerosis sudden complete blindness can occur with no lesion of the eye visible with the ophthalmoscope. The most plausible explanation seems to be supposed vascular changes in the occipital lobes.

[1] E. G. Loring: Medical Record, N. Y., 1886, pp. 79, 80.

[2] Lancereaux: Schmidt's Jahrb., vol. ccviii. p. 137.

[3] "Maladies du Cœur et des Vaisseau;" Huchard: Paris, 1889, pp. 219, 350.

[4] Koenig: Op. cit., Paris, 1890.

Fibrous myocarditis is a common lesion following the occurrence of this change in the coronary arteries. It is not long since a sudden death came under my notice in the person of a prominent surgeon from the supervention of thrombosis upon the existence of those two lesions in the structure of the heart. Thrombosis is exceedingly common in consequence of the roughening of the arterial wall which is frequent in advanced conditions of this lesion.

The various consequences of fibrous myocarditis, from the functional disturbances which it causes to the development of cardiac aneurism, need not occupy our time. Much interesting material upon this subject has been collected by Lüttich, of Hanover, in *Schmidt's Jahrbücher*, vol. ccvii. p. 22. The most important paper there quoted is by Leyden.

It is not at all necessary for the muscular structure of the heart to have become degenerate as a consequence of sclerosis in order to account for sudden death occurring from the sudden stoppage of a coronary artery.[1] The heart-muscle may be healthy or even hypertrophied under these circumstances.

In slowly developing conditions of fibrous myocarditis the heart may become very extensively diseased before serious symptoms result, and death may occur only after protracted feebleness and suffering. Acute thrombotic softening, or hemorrhagic infarction in the myocardium can occur in consequence of sclerotic thrombosis of a coronary artery. This lesion occurs most frequently in the wall of the left ventricle, and is the commonest cause of rupture of the heart. When the heart-muscle is degenerate in association with lesion of the coronary arteries, we are apt to find the fibrous change in it to which reference has just been made. Fibrous masses may be diffused through the muscle, or there may be only a circumscribed area of such tissue. In this latter case it is usually situated in the left ventricle, near the apex, and is not seldom the origin of a cardiac aneurism.

The symptomatology of fibrous myocarditis is of extreme interest, but would take us a little too far from our subject.

Demance[2] has published four cases of disseminated spinal sclerosis

[1] E. Leyden: Zeitschr. f. klin. Med., 1884, vii. 5 u. 6.

[2] Revue de Méd., 1885, Nos. 1 and 7; quoted in Fortschritte d. Med., 1885, p. 186, and 1886, p. 64.

associated with general arterio-sclerosis. In some of these the arterial lesion is most pronounced in the cord. Miliary aneurisms are common, and hemorrhages into peri-vascular spaces. In one case a copious hemorrhage occurred in the cervical cord. A perusal of his cases would lead to the belief that the disease which he describes differs in its symptoms as it does in its etiology from the ordinary disseminated sclerosis. Mendel[1] claims to have found arterio-sclerosis in several small branches of the middle cerebral in a case of progressive paralysis of the insane. He believes that it may be the indirect cause of hydrops of the peri-cellular spaces, causing congestion of the lymphatics, in consequence of its disturbing influence over arterial and venous circulation. He thinks, apparently, that it may be a frequent (possibly essential) lesion in progressive paresis.

Numerous instances are recorded of serious disturbances of nutrition of the extremities associated with this lesion of the arteries. Will[2] narrates a case in which gangrene occurred in both upper extremities from finger-tips to middle of forearms. The patient was fifty-two years old, not syphilitic, and no other causative influence could be found. This is said to be the third carefully examined case of this kind. Hutchinson[3] and Klotz[4] ascribe gangrene of lower extremities to this lesion and record cases in point. It seems not unlikely that this condition may have more to do with senile gangrene than has been supposed. D'Ornellas[5] describes a case of gangrene of the fingers in a syphilitic, necessitating amputation. The patient was forty-five years old, and had been infected by syphilis twenty years previously. Pulse was absent in radial, ulnar, and palmar arch, as well as in lower third of brachial. The arteries felt like tough cords. Under specific treatment the patient made a good recovery, except so far as the loss of his fingers. He was seen by Fournier, Verneuil, Duplay, and others, who concurred in the diagnosis.

Hutchinson[6] describes a case of senile obliteration of temporal arteries in a man eighty years of age, apparently due to sclerosis.

[1] Berliner klin. Wochenschrift, 1883, 17; quoted in Fortschritte d. Med., 1883, p. 330.

[2] Berliner klin. Wochenschrift, 1886, xxiii. 17; quoted in Schmidt's Jahrb., ccx. p. 167.

[3] Archives of Surgery, London, 1889-90, i. 323.

[4] New York Medical Journal, October 8, 1887.

[5] Ann. de Derm. et de Syph., ix. p. 35.

[6] Archives of Surgery, London, 1890-91, ii. p. 54.

The vessels felt like hard cords. While the process was going on there were much pain and tenderness in them, both of which disappeared when it became complete. There was no gangrene nor any other symptom than those mentioned.

Thoma's[1] discovery of the presence of Pacinian bodies in arteries explains the occurrence of pain as a symptom of arterial disease. He believes that many of the rheumatoid pains which occur in the chest in people from thirty-five to forty-five years of age are to be thus explained. Thus also he explains the pain produced by a beginning aneurismal dilatation, before it is large enough to press upon surrounding parts. By their involvement one would explain the acute pain produced by the lodgement of an embolus in a peripheral artery.

Phlebo-sclerosis.—Of late years evidence has accumulated which goes to show that a similar lesion exists in the veins. A paper by Sack[2] is instructive as showing its relation to the lesion in the arteries. It is shown that the two sets of vessels are likely to be simultaneously affected in the same individual, and the lesion in the veins, probably, does not differ in etiology from the arterio-sclerosis.

According to Sack, phlebo-sclerosis occurs most commonly in the lower extremities, as is also true of the arterial lesion. He ascribes its frequency in this location to the sluggishness of the circulation here and to variations in blood-pressure. Not only in general, from their dependent position, is the circulation less active in the lower extremities than elsewhere, but there are likely to occur local causes of congestion in them, such as ascites, pregnancy, heart disease, etc. The nodose form does not exist in the veins. When dissiminated patches are found in them, it is likely that they represent the beginning of the diffuse form.

Pokrovsky[3] has also published an elaborate paper on phlebosclerosis. He claims that this is a nodose form of the affection, and that many consecutive changes and degenerative processes follow and accompany it. Spillmann,[4] of Nancy, has written lately on the same

[1] Centralblatt. f. klin. Med., 1889, p. 29.
[2] Virchow's Archiv, 1888, cxii. p. 403.
[3] St. Petersburg, Inaugural Diss., 1890, and London Med. Recorder, 1890, p. 302.
[4] Gazette de Méd. et de Chir., 1890, p. 480.

FIG. 2.

Longitudinal section of left vertebral artery showing arterio-sclerosis with syphilitic peri-arteritis. Other arteries at base of brain showed similar lesion, and there was thrombosis of basilar, which caused death. Patient was forty years of age, and had suffered from intermittent severe headache for a year. He died untreated. *a*. Thickened intima. *b*. Lamina elastica. *c*. Media. *d*. Adventitia. *e*. Small artery of adventitia, showing same lesion.

subject. He quotes extensively from a thesis by Henri Thiebaut,[1] who seems to have devoted much time and attention to this subject.

Although numerous writers concur as to its existence and distribution, no one seems yet to have been able to trace to it any grave consequences. Similar lesion has been also found in the capillaries. Here the disturbance of function produced manifests itself by an increased permeability of their walls, in consequence of which œdema of the tissues results.

The process seems to be so widely spread throughout the vascular system as to justify the name angio-sclerosis which several observers have applied to it.

[1] Thèse de Nancy, 1890.

ON THE RELATIONS BETWEEN ARTERIAL DISEASE AND TISSUE CHANGES.

By WILLIAM T. COUNCILMAN, M.D.,
OF BALTIMORE.

I HAVE thought it would be best in the consideration of a subject which embraces so much, to confine my remarks to a study of diffuse arterio-sclerosis, because, not only on account of the importance of the disease, but on account of the extent of the lesions both in the vessels and tissues, it best serves to illustrate the relation of these changes to each other.

It would not be within the scope of this article to attempt to give anything but a very brief reference to the most important publications which have appeared on the subject. When we leave out of consideration the earlier articles on diseases of the arteries, which relate almost exclusively to the histological details of the changes, the first article in which, along with arterial disease and dependent on this, various lesions of the tissues are recognized, is that of Gull and Sutton, published in 1871. They describe, under the name of arterio-capillary fibrosis, a general disease characterized by the formation of a peculiar hyaline fibroid substance around and in the walls of small arteries and capillaries. This hyaline substance is sometimes homogeneous, sometimes slightly striated. They first describe the changes which take place in the kidneys. In the affected vessels outside of the muscular coat the hyaline fibroid substance forms a layer thicker than this. The vessels are rendered thicker, more tortuous, and the lumen is often encroached upon or completely obliterated. The tubules of the kidney are atrophied, dilated into cysts, and the epithelium finely granular, shrunken, and wasted. The hyaline fibroid tissue appears to commence in the outer coats of the arteries and in the capillary walls, and from these it extends around the glomeruli

and the tubules. By the contraction of this substance the vessels are compressed, the blood-supply in different parts is diminished, and atrophic changes result, or, at the same time with the changes in the vessels and interstitial tissue, changes may be taking place in the cells. The result of the pathological processes in the kidney is the granular contracted kidney. Changes identical to those in the vessels of the kidney are found everywhere, and are especially well marked in the pia mater. In all these tissues the change begins in the adventitia of the vessels and extends into the surrounding tissues and often toward the lumen.

Gull and Sutton differ in their conception of the arterial change from Johnson, who claimed that only the muscular coat of the arteries was thickened. They recognize the fact that in the larger arteries the intima is often thickened and that the nuclei of the muscular layers do not stain distinctly. While the changes in the kidneys are the most marked and the symptoms during life are most indicative of renal disease, they do not constitute an indispensable part of the process. When the larger arteries are affected the intima is also much thickened, and the nuclei of the muscular fibres do not stain well. The heart is always hypertrophied, and this is due to the vascular changes. The disease commonly begins in the kidneys, but in some cases they are but little, if at all, affected, while the change may be far advanced in other organs. It will be seen that the great value of this article of Gull and Sutton's is, that they claim the whole as a general disease of the vascular system. There is no doubt that their general conception of the pathological histology of the process is wrong.

Next in importance to this work of Gull and Sutton is that of Thoma, who, in a series of articles in Virchow's *Archiv*, has considered the whole subject of arterial changes and the laws under which they take place. It is difficult to find in the whole domain of pathology any work more thorough and painstaking than this of Thoma's; in fact, the extent of it and minutiæ with which every idea is followed out, and the further difficulty which the reader has in following the ideas of Thoma, will always stand in the way of its becoming popular reading. He starts out with the study of the fœtal aorta and the changes which take place in this after birth as the result of the occlusion of the ductus Botalli and the umbilical arteries. In the last

weeks of fœtal life the umbilical arteries are the most important branches of the aorta, and, in consequence of their closure, there must be a considerable variation between the width of the aorta and its various branches, although this is partly compensated for by the widening of the arteries of the stomach, kidneys, and intestines. This disproportion between the aorta and its branches extends from the umbilical arteries up to the ductus Botalli, and he finds that, strictly limited to this part of the aorta, there is a formation of connective tissue in the intima by which the width of the vessel is reduced to a normal relation.

This formation of connective tissue he thinks is due to a slowing of the circulation in the abnormally wide vessels, and he asserts, as a general law, that when there is an abnormal relation between the size of an artery and the territory which it supplies, a compensating endarteritis is set up which brings back the relations to the normal standard. He explains in the same way, the endarteritis which takes place in the arteries of an amputated extremity, or in arteries everywhere as soon as there is a disproportion between their calibre and the amount of tissue they supply.

In his studies on arterio-sclerosis he makes two forms. One of these he calls primary arterio-sclerosis, and here the process is set up by local changes in the artery affected which lead to a dilatation, and in consequence of this and in accordance with the law, an increased formation of connective tissue in the intima tends to reduce the artery to normal relations. The other form is the secondary arterio-sclerosis, and this is due to changes in the arterial wall caused by increased resistance to the flow of blood in distant organs. In every case it is the slowing of blood-current and the dilatation which brings about the connective-tissue formation. It is this second variety which corresponds to the disease described by Gull and Sutton. In all these cases the primary change in the vessels is a degeneration of the media. In the aorta it is this degeneration which allows the vessel to dilate, and in consequence of this dilatation the sensitive nerve-endings in the vessel's walls, the Pacinian corpuscles, are irritated. This leads to a dilatation of the vasa vasorum, and an excitation of the trophic nerves, causing a new formation of connective tissue. This explanation of the process must be considered extremely hypothetical, and one for which there is no analogy in pathology. It will be seen from

this that Thoma supposes the changes in the aorta in the second variety to be only the result of changes in the arterioles of distant organs. The nodular form of arterio-sclerosis is due to circumscribed dilatations of the arteries and a new formation of connective tissue which exactly fills out the dilated area. When such arteries are examined after having been injected with paraffine under a pressure of 16 cm. of mercury, the raised plaques which are so prominent in the uninjected vessels have entirely disappeared, leaving a smooth intima — the primary changes here having been a local dilatation and a local increase of connective tissue which compensates for the dilatation.

Our study of arterio-sclerosis, in which we have been associated with Dr. W. T. Howard, is based on the examination of forty-one cases which have been autopsied at the Johns Hopkins Hospital since its opening, two and a half years ago. These can be divided into three classes. In such a division we are beset with the difficulties which always accompany a classification of pathological conditions based on anatomical lesions alone. While we undoubtedly find typical cases of each class, many cases are seen which cannot be brought under hard and fast lines of division, but represent more or less mixed forms, and must be placed in the class to which the more prominent changes belong. The first of these divisions, the nodular form of arterio-sclerosis, has little interest for us. In this the changes are limited to the aorta and large arteries, and we find along the course of the vessel, which is otherwise smooth and of normal calibre, elavated plaques, sometimes translucent and cartilaginous in appearance, sometimes calcified or softened. The description of Thoma applies perfectly to these. The growth is entirely within the intima, and the media at the point affected is thin and degenerated.

The second form is the senile endarteritis. In the most typical cases of this the aorta and all the larger arteries are converted into almost rigid calcareous tubes. The inner surface is rough, and there are frequently fissures and losses of substance to which thrombi may adhere. The arteries are not only irregularly dilated, but they are elongated as well, this being seen in the formation of curves in the course of the artery where none normally exist, and in the marked accentuation of normal curves. Notwithstanding the extent of the calcareous infiltration, the walls of the arteries are thinner than

normal. The heart is small, often showing the condition of brown atrophy, and there are similar atrophic changes in the other organs, best marked in the liver and kidneys. The kidneys are smaller than normal, their color little, if any, changed, the surface slightly granular with frequently depressions of greater depth in places where a more extensive loss of substance has taken place. On section of the kidney it is seen that both cortex and pyramids are concerned in the atrophy, the cortex suffering most. On the section the cut ends of the smaller renal arteries project above the surface and are frequently calcareous. On microscopic examination there is both an increase in the connective tissue and atrophy and loss in the parenchyma. The tubules are shrunken or in places converted into cysts, the epithelium smaller and more granular, the glomeruli are in general small, and many of them show all stages of atrophy. When fresh sections of the organ are examined, there is always some fatty degeneration of the epithelium, though often slight in amount. The connective tissue is dense and contains relatively few granulation-cells.

The changes in the liver are very analogous to those in the kidney. There is some atrophy, the organ not weighing more than 1000–1200 grammes, the surface is smooth or slightly wrinkled, and the consistency is increased. On microscopic examination the cells are small, frequently fatty, the capillaries are wider than normal, and there is some increase in the connective tissue. The arteries show lesions very similar to those in the other tissues. There is marked atrophy of all the coats, particularly of the media. The muscular fibres of this become necrotic, hyaline, and finally, by the deposit of calcareous matter in the necrotic tissue, the whole artery is frequently converted into a calcareous tube. The process is strictly one of atrophy and degeneration, and the arteries share in the fate of the tissues generally. In fourteen cases of senile endarteritis, there was entire absence of heart hypertrophy in seven. Of the others, in all of which the heart hypertrophy was of very minor degree, two had diseased aortic valves, and in the other five, the senile changes in the arteries were complicated with other changes which we are about to describe.

The most important class of cases are those belonging to the diffuse arterio-sclerosis, in which the lesions are widely distributed, embracing all the arteries of the body. We are not able to make the sharp distinction here which Thoma does, dividing them into two classes, in

one of which the lesions are local in the vessels and due to local changes, while in the other the lesions in the great vessels are secondary to changes in the small. Contrary to the senile endarteritis, the subjects of this are generally men in the prime of life. In 27 cases of this disease, the youngest, a negro, gave his age as twenty-three; the oldest was sixty. Most of the cases ranged between forty and fifty-five; 14 were white and 13 colored. We find in this disease a very typical pathological picture. Most of the subjects who came to autopsy were strongly-built, well-nourished, muscular individuals. As a rule, there was no œdema either of the face or lower extremities. When œdema was present it had come on in the last few days or weeks of life. Heart hypertrophy is always present and may reach an extreme degree. In two cases in which there were no valvular lesions whatever, the heart in one weighed 850 grammes, and in the other 820. The average weight was over 400. The myocardium is firm and dark. Close examination often shows some degree of fibrous myocarditis, this depending on the degree of involvement of the coronary arteries in the general trouble. The heart hypertrophy may be confined to the left ventricle, but in the most marked cases it is always associated with so much dilatation that the right ventricle also becomes hypertrophied. The dilatation may be so excessive as to affect the integrity of all the valves. Anatomical lesions of the valves are usually absent. There may be some extension of the aortic disease to the aortic valves or the aortic segment of the mitral valve, but the thickening so produced is not generally sufficient to interfere with the functions of the valve. The supposed inflammatory changes in the myocardium described by Buhl and referred to by Thoma, are not found. The most marked changes are found in the aorta and the large arteries given off from this. The large arteries are more or less dilated, the dilatation in some cases starting in the aortic orifice and extending throughout the aorta and large arteries. This dilatation is seldom homogeneous throughout, but in addition to the general dilatation there may be here and there more local dilatations. Some of the measurements of the arteries will show how extensive this dilatation may be. In two well-marked cases the measurements are as follows, the circumference of the vessels being taken in centimetres:

	Case 1.	Case 2.
Just above aortic valves . . .	8	8
In transverse arch	8½	14
In middle of thoracic . . .	7½	9
At diaphragm	6	7
At renals	5	6½
At bifurcation	4½	4

The branches of the arch are sometimes relatively more dilated than the aorta. There is elongation of the vessels as well. The aorta makes lateral curves and the normal curves of other arteries are greatly accentuated. In addition to the dilatation there is a general diffuse thickening of the arteries which is often relatively greater in arteries the size of the radial than in the large. In the large arteries the intima is roughened by projecting elevations which are frequently distinguished by differences in color and consistency. They may be of a pearly, transparent color and very hard, in both color and consistency similar to cartilage. They may be of an opaque, whitish-yellow color, and the centre soft and pultaceous. On incising such places a soft, white, mortar-like mass escapes. We may find irregular, ragged excavations, often covered with fibrin, showing that the softening has extended through the intima of vessel during life. Similar areas of softening and degeneration may be found in the diffusely thickened intima. There may be more or less calcification which is usually confined to the projecting elevations, but this never reaches the same extent here, as in the senile form. There are frequently longitudinal folds and puckering of the intima as though due to the contraction of the vessel after death.

To the naked eye the kidneys sometimes show the most marked lesions, at others the changes are so little apparent that they could easily be passed over. The color of the kidneys varies considerably; generally they are hyperæmic, the extent of this depending upon the greater or less degree of chronic passive congestion which is present. They may not be diminished, or even slightly increased in size; the capsule may strip off easily or be more or less adherent and small portions of the cortex may be removed with it. The surface is usually more or less granular and there are frequently deep depressions showing greater and more localized atrophy. Finally, the appearances may be those of the granular contracted kidney. On section the cortex is generally slightly reduced in thickness and the normal markings

somewhat obscure. The arteries are prominent and project above the cut surface. Even with the naked eye it can be seen that their walls are thicker than normal. The most marked feature of the kidneys is an increased consistency. It is more resistant both to the knife and to attempts to break and tear its tissue.

The liver, to the naked eye, shows little change. It may be somewhat reduced in volume, but generally its weight and dimensions are normal. The capsule is smooth, and the most evident changes are those connected with chronic passive congestion when this is present. It must be remarked that even when a considerable degree of chronic passive congestion is present the changes produced by this in the liver are not so marked as in an uncomplicated heart case. As in the kidney, the most striking change in the liver is the increased consistency. It will be found very difficult to tear or even to thrust the finger into the cut surface, and an increased resistance is given to the knife. The lungs are little, if at all, affected, save by the chronic passive congestion, and the pulmonary artery is nearly always entirely free from disease. There are no noteworthy changes in the other organs save an increased toughness. In several of the cases there was more or less extensive hydrothorax, and in a little less than one-half there was some œdema of the lower extremities. In three of the cases there was general anasarca. Death resulted either from some intercurrent disease or from the arterial lesions alone, and in many cases was sudden. In some of these cases of sudden death, extensive disease of the coronary arteries was found, in others it could not be attributed to this.

The histological examination of the tissues was in most cases confined to the diseased arteries and the liver and kidney. The last two organs were chosen both on account of the importance of the lesions in them, and also from the fact that their tissue offers especial advantages for the study of the small arteries and capillaries. I will spare the Association all the details of the histological changes in the liver and kidney. Briefly, they consist in the kidney, of various degenerative changes in the epithelium, of an increase in the connective tissue, and of widespread lesions in the arteries especially affecting those of very small calibre. The epithelial degeneration consists of simple atrophy of the cells and of granular, fatty, and hyaline degeneration, which is in some cases more focal, in others more diffuse in character.

The same with the increase in connective tissue. This is found both in well-defined streaks running down from the cortex, and in a diffuse thickening of the inter-tubular tissue everywhere. It is, of course, most marked in the regions which correspond to the greatest atrophy of the cortex, shown by the deep depressions on the surface. In these places only remnants of the epithelial structures of the organ are found.

In this connective tissue, tubules in every stage of atrophy can be seen, some entirely collapsed, others irregular in shape, containing but a few degenerated cells, others, again, dilated into small cysts; from these larger bands of connective tissue smaller masses are given off. There is also some diffuse connective-tissue increase. The cells in this newly formed tissue vary considerably in number; in some cases it is dense and contains very few cells, in others it contains numbers of round granulation-cells. There is always a marked change in the arteries, which is always more marked in the smaller ones. The most prominent change is a thickening of the wall, which is due to the formation of a homogeneous hyaline tissue within the muscular coat. This tissue usually contains but few cells, is faintly striated, and stains a light brown with the osmic acid used in the hardening solution. In many of the smallest vessels nothing can be seen of the elastic lamina, in others only fragments of it can be made out, in others it is preserved. The lumen of these most affected arteries is seldom perfectly round, but the newly formed tissue makes irregular projections into the lumen, deforming it in various ways. The muscular fibres of the media show the most marked atrophic changes. Fatty degeneration of the cells can be made out both in the fresh sections and after hardening in Fleming. The nuclei are often very thin and atrophic-looking; vacuoles are sometimes seen in them. In some arteries the nuclei have almost entirely disappeared and the media is changed into a homogeneous tissue very similar to that in the thickened intima. On longitudinal sections of the arteries these changes in the intima were sometimes very apparent. In places where the muscular coat was at first sight but little, if at all, affected, a close examination showed it to have a reticular appearance, a dark-brownish substance forming the reticulum, leaving round spaces between, which correspond to the muscular fibres and in which the muscle nuclei are frequently seen. The tissue between the muscle-cells passes directly into

that of the thickened intima. In the larger renal arteries there is always some degeneration of the media, but it is not so well marked as in the very small.

The glomeruli are variously altered. Many will always be found completely atrophied and converted into a mass of dense hyaline tissue, which contains a few stellate or spindle-shaped cells. In nearly all of them the most marked feature is a thickening of the capillary walls The thickened capillaries are homogeneous, refractive, and similar to the tissue forming the thickened intima of the small arteries. In places this thickening proceeds to complete obliteration of the vessel, so that in the glomerulus there are areas in which no capillaries are found, the space being filled by a dense tissue containing small, irregular, and brightly staining cells. The cells of the glomerulus are in the early stages increased in number, both the cells of the blood capillaries and the cells of the covering epithelium. In one case the increase in the epithelial cells was particularly well marked. In many cases there was a growth of connective tissue into the glomerulus which seemed to take place from the adventitia of the vessels of the root. The atrophy was brought about both by the occlusion of the vessels and by the advancing growth of the connective tissue. Coincident with these atrophic changes in the glomeruli and keeping pace with them there was a thickening of the capsule.

In the liver, in one of the best marked cases, there is some increase in the connective tissue in the portal spaces. The arteries show essentially the same conditions as those of the kidney—there is the same growth of tissue in the intima, and the same degeneration of the media. The liver-cells in general are much smaller than normal; they are often fatty, and a few completely necrotic cells were found. The spaces between the rows of liver-cells are broader than normal. The most striking change in the liver is the thickening of the capillary walls by a tissue very similar to that producing the thickening of the glomerular capillaries. To this tissue the marked resistance and toughness of the liver is due. It is homogeneously distributed all through the liver, but in some places is much more abundant and much denser than in others, and from these areas it seems to radiate out in all directions. The capillaries are but little reduced in diameter, all the thickening apparently taking place outside of the vessel between it and the rows of liver-cells. Sometimes processes from this tissue were given off

which penetrated between the cells. Another marked feature which was so often present in these livers as to almost constitute an integral part of the changes, was a fatty degeneration of the stellate cells. These peculiar cells, first described by Kupper, lying outside of the capillaries, between them and the liver-cells, give a remarkable appearance to the fresh sections. The section appears to be sprinkled with dark stellate figures. In one of the livers there were sharply circumscribed foci of necrosis, and in the capillaries between the rows of necrotic cells and outside of the capillaries between the cells themselves were immense numbers of leucocytes.

The histological changes in the aorta and the larger bloodvessels are very analogous to those which we have described as taking place in the smaller. They present such manifold variations that it would take us too long to enter into a complete description of them. The two essential changes are various degenerative changes in the media and a growth of tissue in the intima. The degenerations in the media are shown in various ways. Sections of the fresh artery show some fatty degeneration, but this does not play the chief part. The most common change seems to be necrosis and hyaline degeneration. The muscle-cells lose their nuclei and the whole muscular coat is changed into a solid homogeneous mass. Even the elastic fibres between the muscle laminæ are frequently broken up and disappear. In some sections of the dilated carotid, the media as such could not be recognized, the whole artery being changed into a dense, thick mass of sclerosed connective tissue. This atrophy of the media is always best marked opposite the points of greatest thickening of the intima. The tissue composing the thickened intima consists of thick layers of dense connective tissue, which not only in consequence of the poor nutrition which it has, but also in consequence of the pressure to which it is subjected, is particularly prone to degenerative changes. The tendency to degenerative changes, however, is not so marked here as it is in the senile form.

This diffuse arterio-sclerosis which we have described agrees best with the form which Thoma has described as secondary arterio-sclerosis, and in which he considers that the changes in the large arteries are due to the resistance to the blood circulation which the diseased small arteries causes. In a paper on the conditions of the vessels in Bright's disease, which preceded his publications on the arteries, he shows that there is an opposition to the passage of the

blood, which is due primarily not to a narrowing of the calibre of the vessels by the thickening of the intima, but by an increased permeability of the vessel walls. With this disease of the vessels there is an increase in the connective tissue and destruction of large numbers of capillaries, still further diminishing the size of the vascular bed, and then comes a disparity between the calibre of the artery and the territory to be supplied, followed by a compensating growth of connective tissue. This endarteritis of distant organs is extended in the same way to the aorta. We would rather take the view that the changes in the aorta and in the minute arteries are due to the same cause; that in the diffuse endarteritis we have a disease which is primarily due to a degeneration of the muscular fibres of the media. On this the growth of the intima follows, which is due to the same cause acting in two ways: in one, by the well-known law of connective-tissue growth, to supply a defect, in this case the degeneration of the media; and in the other, possibly acting under the law of Thoma, a compensating endarteritis to restore the abnormally dilated vessel to a normal calibre. Thoma's assumption that his secondary arterio-sclerosis is due to an increased blood pressure in the aorta from the increased peripheral resistance cannot be proven. On the contrary, we know that we may have heart atrophy with regurgitation at the aortic orifice, where the pressure in the aorta is certainly momentarily increased, without any affection of the intima. In this case we might suppose that the sudden pressure, followed by relaxation, would be fully as injurious to the media as continued pressure. We know further that we may have continuous increased pressure in the aorta from peripheral resistance without any degeneration of the media and without any arterio-sclerosis. Examples enough are furnished of this in various renal lesions with heart hypertrophy. It is probable that increased pressure alone will not affect the media, and the integrity of the vessel can be preserved.

There can be no doubt that this secondary compensating endarteritis of Thoma plays a most important part in pathology. We find it, as Thoma has shown, in an artery the area of whose bed of distribution has been diminished or destroyed, whether by a destruction of tissue, as in the case of an infarction, or in an amputation stump. In the cases of this, however, which we have seen, there was the great difference from the primary process, in that the media was intact in

most, and certainly in the most recent cases, the growth apparently taking place from the intima without any destruction of media. The change which finally takes place in the media is the slow atrophy of an unused tissue. Not only do we find this growth of the intima following degeneration of the media in the diffuse arterio-sclerosis, but we find it in the nodular endarteritis in whatever way produced. In a case of syphilitic endarteritis reported by Thomas, in which gummata were found in the walls of the vessels, there was a growth in the intima, always most intense opposite the affected wall.

Are the changes in the kidney and liver the result of the arterial changes? We think they are. While in advanced atrophy of the organ, from whatever cause, we have some thickening of the vessels which is of the nature of Thoma's compensating endarteritis, they are not so prominent as they are in these cases, nor are they of the same nature. The changes in the arterioles and glomeruli of the kidney, and the arteries and capillaries of the liver, are too distinctive to suppose that they are secondary. We do not find similar changes in the bloodvessels of either organ when we have every reason to believe that the lesions are due to other causes. In cirrhosis of the liver there may be some thickening of the intima of the vessels of a compensatory character, but the lesions consist rather in thickening of the adventitia than the intima, and the lesions of the media are absent.

The affections of the kidneys are both general, and there are foci of more intense atrophy where there are large defects similar to those left by infarctions, and we find in the most advanced disease sometimes complete occlusion in the corresponding arteries. The nature of the atrophic lesions in the epithelium do not offer us any certain criterion to judge by. We may find fatty and hyaline degeneration of the epithelial cells in a variety of conditions, but we are not so apt to find simple atrophy, diminution in size of cells, so marked in other conditions. The increase in the connective tissue also is not distinctive. It follows atrophy here, as in all other places. That it does follow and not precede atrophy can be seen best on a close study of the glomeruli; we find thickening of the capsule and growth of the surrounding connective tissue, and atrophic changes in the vascular tuft at the same time. We find the earlier stages of these changes in the capillaries without any change in the capsule,

but we do not find the thickening of the capsule without any changes in the tuft. The nutrition of the kidney is probably more interfered with by the disease of the glomeruli than in any other way; for it must be remembered that all the renal blood, with the exception of that provided for by the few anastomoses, passes through the glomeruli. The closure of the capillaries is in part compensated for by anastomoses of the glomerular vessels with the vessels of the capsule, and by dilatation and closer anastomoses of some of the loops.

It would be difficult to conceive of any series of pathological conditions so closely bound together, and in which every lesion so tends to intensify some preceding lesions, as we have given us in this disease. First, the arterial changes, producing not only resistance to blood circulation with increased pressure and heart atrophy, but changes in the tissue of the kidney, interference with its proper functions, and the still further increase of blood pressure and heart hypertrophy in consequence of this. We must add to this the effect on the circulation of an overloaded venous system, due to the chronic passive congestion which is almost sure to come on sooner or later when the valves are incompetent for the dilated heart.

We think that these lesions which we have described should be clearly separated from the senile endarteritis and the lesions accompanying this. The senile endarteritis is a disease of advanced life, seldom occurring before the age of fifty. The lesions in the vessels are slow, and there is little reaction to the degeneration. While the tissue-changes are probably in part dependent on the arterial lesions, the close connection cannot be traced. Clinically, there is absence of the high arterial pressure which constitutes the most obvious clinical manifestation of the diffuse arterio-sclerosis. The diffuse arterio-sclerosis is a definite disease; the lesions in the arteries and tissues form a pathological entity, and the primary lesion to which all the changes are due is a degeneration of the tissue of the media of both the large and smaller arteries.

Fig. 1

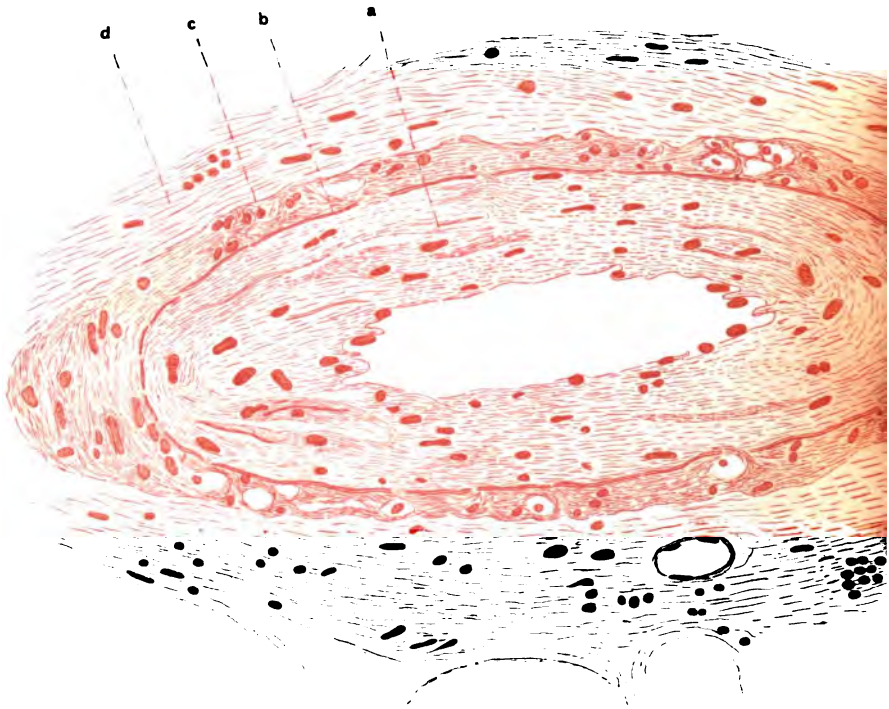
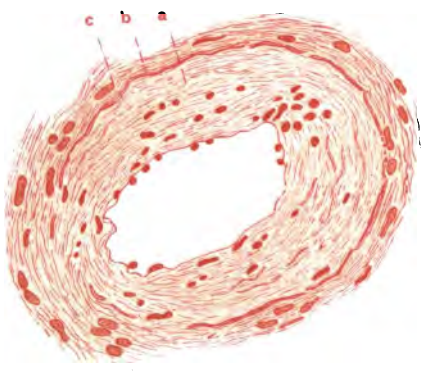


Fig. 2'



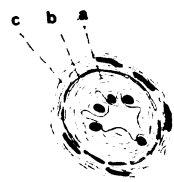
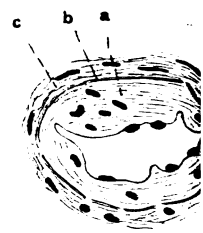


Fig. 2"

Fig. 2'''



W.T. Councilman Del

Fig. 4

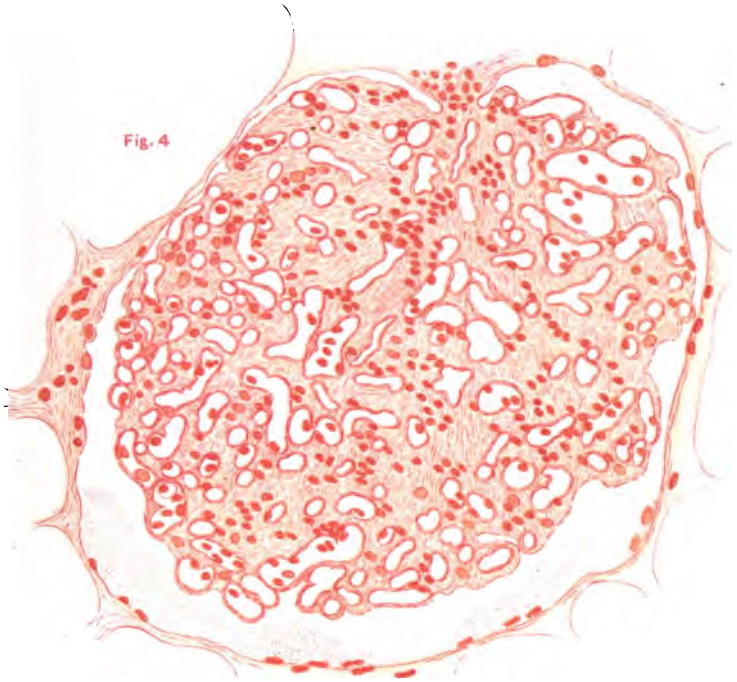


Fig. 3

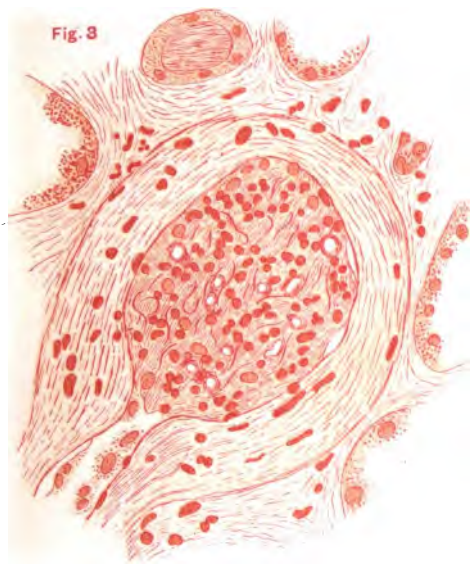
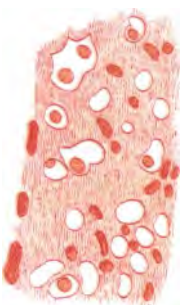


Fig. 5



A. Hoen & Co. Lith.

Description of Plate.

Fig. I.—Oblique section of a small artery in the kidney. *a*, thickened intima; *b*, elastic coat; *c*, muscular coat; *d*, surrounding connective tissue. The most marked change is seen in the thickening of the intima and the degeneration of the muscular coat. The elastic lamella is broken in places and the folds are lost.

Fig. II.—The two smallest of these arteries are from the liver; the larger from the kidney. In the smallest arteries the lumen is very narrow and irregular. The intima is very much thickened, and the muscular coat can hardly be recognized as such. In the upper figure the elastic lamella has disappeared in one portion of the vessel.

Fig. III.—Glomerulus in an advanced stage of atrophy. The vessels are almost entirely obliterated, the whole is greatly shrunken, and the wall of the capsule is thickened.

Fig. IV.—A glomerulus in an early stage of atrophy. The walls of the capillaries are thickened. The lumen of many of them is very small and irregular, and there is considerable connective tissue growing between them. In places this connective tissue is rich in cells. There is little or no shrinkage of the glomerulus, and no thickening of the capsule. The granular material in the space between the glomerulus and the capsule is coagulated albumin.

(Figs. I., II., III., IV. are all drawn with camera lucida. Zeiss obj. d.ocl. 2.)

Fig. V.—Small portion of the muscular coat of a larger artery, more highly magnified. The spaces in this mark the degenerated muscular fibres. Between these is connective tissue very similar to that forming the thickened intima.

DISCUSSION.

Dr. William M. Ord, of London: I can assure you that I have listened with great profit, as well as with great pleasure, to the admirable and most comprehensive papers which have been read. I could not pretend to criticise them in any detail or with any effectiveness. But perhaps some of my experience with certain forms of arterial disease, in one particular line of observation in England, may be interesting. Both papers have spoken of Sir William Gull and Dr. Sutton's important communication on the subject of arterio-capillary fibrosis. I think, perhaps, I would differ from those who maintain that the appearances described by Sir William Gull and Dr. Sutton were due to the use of particular media, such, for instance, as glycerin. I have seen again and again, in cases of contracting granular kidney, all the changes well illustrated in the vessels of the pia mater, both in arteries and capillaries, perfectly presented, when in the preparation no glycerin whatever had been resorted to, where the hardening was either by alcohol or

Müller's fluid, and the ordinary staining and mounting processes had been adopted. There, in a series of specimens, one has found what has already been described—the change in the adventitia, the change consisting in great increase of fibrous matter of remarkable translucency; change in the media with signs of degeneration of the muscular fibre, due apparently to interpenetration of this fibroid material between the cells, and change of equivalent kind in the interna: the whole having the result of an enormous comparative thickening of the arterial or capillary wall and corresponding diminution of the lumen of the vessel. Of course, since that hypothesis was started, the question has been whether such changes in the arteries and capillaries were the result of the renal disease or were part of the cause of it, or were a part of a disease affecting the whole system, perhaps most characteristically seen in the kidneys, on the one hand, and in the arteries on the other. For my own part, long observation had inclined me to think that it is not merely a disease of the arteries or kidneys, but a general disease affecting the whole system, and I regard it as very closely associated with gout—gout depending on injudicious feeding, to a large extent, in the way of both food and drink.

In my earlier practice I was in a suburb of London frequented by wealthy citizens who, after their day's work, would go home and partake heartily of meats, and wash the meats down with liberal libations, perhaps of claret, or sherry, or port, afterward winding up with whiskey and water. These men did not get drunk, perhaps a little top-heavy, but they went on with this kind of life week after week and year after year. I can certainly recall at least twenty of such men, one after another, who fell away in middle age, hardly any of them reaching sixty, with symptoms which began in more or less of a gouty fashion and ended with distinct contracting granular kidney. I can think of one of them now, a very hearty man, by no means an intemperate man, but still a man who lived well. He for years had gout. For years he had from time to time attacks in the night of what he called asthma, which I took to be rather anginous. He had distinct thickening of arteries wherever arteries could be felt. He had distinct hypertrophy of the left ventricle; he had from time to time epistaxis. Yet I examined that man carefully over and over again before any signs that the urine could give of the existence of any change in the kidneys were found. I was so much interested in him that I got Sir William Gull to see him with me. This was just before his paper appeared. We both came to the conclusion that he probably had arterio-capillary fibrosis, and that ultimately we should get the evidences of contracting granular kidney. So, indeed, we did. Two years before his death he began to pass albumin, and we found casts and other signs of renal change; he became dropsical, gradually failed, and died.

The association of this form of disease with gout has been, in my practice, very much presented to me. Some years ago I asked our demonstrator of pathology at St. Thomas's Hospital, London, to examine the great-toe joints in a series of people, aged between forty and sixty, with regard to the pres-

ence in them of a deposit of urate of soda. They examined for me about one hundred and thirty cases taken hap-hazard, and they found deposit in seventeen cases. They rejected very young people, taking only the middle-aged and elderly. Of these seventeen who had deposits in the great-toe joints, twelve had unmistakable contracted granular kidney, often very pronounced; and in the remaining five there were in all changes in the kidney of an allied nature. Not always was there only contracted granular kidney, but composite changes, in which it was clear that arterial degeneration took a considerable part. Very often we have been accustomed to think of gout as a sort of inheritance to be laughed at or to be proud of, as the case may be. But I may say that, since that series of observations, I have come to look at gout with much more seriousness than before, and to regard it differently in relation to life insurance. I suppose, as far as I can make out, your opportunities of seeing these things are not so great in this country as they are in England, owing to the more temperate life of your middle classes, in this and especially the succeeding generation.

I should like to ask one question. Am I quite right in supposing that the specimen "H," shown by Dr. Peabody, was taken from a boy dying of cerebral hemorrhage? And what was the source of the hemorrhage in that case?

DR. PEABODY: I regret to say that I cannot answer the questions definitely, as the case occurred some ten years ago, at a time when I was not particularly interested in this subject. I think that death was due to a miliary aneurism.

DR. ORD: We do not get, as far as I know, cerebral hemorrhage of large bulk in the young without aneurism, either miliary or larger. I will inflict one case upon you: A boy under my care had obscure symptoms. He had a partial left hemiplegia when admitted to the hospital, and a good deal of mental affection and one very curious symptom, which I certainly think was not shammed, namely, a uniocular diplopia, or at all events he described such a thing without anybody having prompted him to do so. This boy left comparatively well, and I docketed him with "cerebral tumor," with a note of interrogation. He came in two years afterward for an abscess in the neck, and died quite suddenly. It turned out that he had a very large clot in the right cerebral hemisphere. In the centrum ovale majus there was a clot two inches long and one inch in diameter, the shape of a smooth sausage, a partially organized clot enclosed in a cyst which disturbed the symmetry of the brain. Seeing this clot, and finding that there were changes in the arteries, they being thicker than they should be in a child of that age, I asked the demonstrators to look for an aneurism. They looked and found none. I went home and thought about the case and then went down to the museum, for the specimen had passed from the demonstrator to the curator. As the specimen was a good one, he did not want to meddle with it, but I said he

must look for an aneurism. On this third search was found an aneurism about the size of a pea, which communicated by a slit-shaped orifice with the cyst containing the blood-clot, and was manifestly the source of a hemorrhage. I think, both with regard to a great deal of cerebral hemorrhage and also to a great deal of pulmonary hemorrhage, we must still refer more and more to aneurism as a source of the bleeding.

DR. WILLIAM GAIRDNER: Dr. Peabody has spoken of the subject of aneurism in relation to arterio-sclerosis, and I was expecting that he would speak of the dissecting aneurism which has always seemed to me to have an interesting bearing on the behavior of the arteries to those forces which, acting upon their coats from within, in all probability give the first impulse to local dilatations; forces of the mechanical kind, probably, tending to the production of aneurism in the individual. At the same time, the fact that Dr. Peabody did not allude to the subject of dissecting aneurisms will perhaps give more scope for my present remarks.

My attention was directed to dissecting aneurism very early in consequence of the researches of a very well-known writer of that day, the late Dr. Peacock. I got from Dr. Peacock distinctly the notion that dissecting aneurism, in all probability, had some relation to strain of the inner coat of the artery; and the peculiarity of dissecting aneurism is that the inner coat becomes severed as by a rupture or injury, and the blood in that way is admitted to free communication with the middle coat, and instead of forming a pouching aneurism it dissects the fibres of the middle coat sometimes for many inches along the artery and thus makes a pathological dissection of the coats of the vessel. Now ever since having my attention directed to that fact, I have always said to myself that there must be some reason for it, in particular cases; dissecting aneurism being, if not extremely rare absolutely, at least very much more rare than the sacculated form. While in this state of mind, a great many years ago, and looking over the great museum then at Chatham, now at Netley, Southampton, I found a preparation which had been described in print, and which seemed to me to be one of those single preparations which tell a great deal. It was the case of a young negro, supposed to be an extremely athletic and powerful man and in very good health, who leaped down from a wall, a distance of fifteen or sixteen feet, and lighting upon his feet received a shock which in a very short time brought his life to a close. His body was opened and the inner coat of his aorta was found to be torn straight across for half an inch or so, then the blood had started a separation of the fibres of the middle coat for an inch or two, and then a new rupture of the outer coat, opening into the pericardium at a point two or three inches from the point of the internal rupture. There, thought I, was a dissecting aneurism shown in the very act of its production in a very short period, and that in an artery that was not visibly diseased. Putting these things together it seems to me likely that if a strictly healthy artery torn in this way under strain may lead to dissecting aneurism, that in arteries which have not

undergone much degenerative disease, but in which the inner coat is brittle, or gets accidentally ruptured, the result may be, in certain cases, a dissecting aneurism; and if there was much softening of the middle coat, and if the strain was not such as to lead to a positive rent, that the same kind of strain which produced in the first instance rupture of the vessel might probably result in a bulging of the middle and inner coats, and that bulging once produced would lead to agglutination of these coats so as to protect them against the dissecting process, but, on the other hand, to expose them still more to irregular dilatation; and that gradually by the force of the blood any such dilatation would become sacculated, and enlarge into an aneurism. In diseases of the arterial coats, as in almost every other kind of pathological change, we always observe degenerative and destructive lesions going on side by side with processes of repair often more or less imperfect; arterio-sclerosis is no exception to this, as Dr. Peabody has well pointed out. I was not prepared by my pathological experience for his apparently precise statement that the period of degenerative change, during which the liability to aneurismal protrusion is likely to be established for the first time, extends over about a year; but it may well be so. At all events, it is a matter of daily experience, that in the very advanced stages of arterio-sclerosis, when the greater arteries are not only degenerated throughout, but infiltrated with calcareous matter, aneurisms are relatively rare; it may, therefore, be taken as probable that atheromatous infiltrations pass in this way toward a kind of healing; one, no doubt, which is not only incomplete, but is fraught with new kinds of danger to life. All these facts and reflections have been familiar to me (as to all others who have commenced as pathologists) during the whole course of my life as a hospital and general physician.

I am only endeavoring to explain a state of mind that has prevailed with me for forty years, and under which I have been always observing individual cases. Only one of these cases is, perhaps, worth alluding to. I was called, some years ago, down to a town in Ayrshire to see a gentleman in extreme distress. He had had a sudden fainting, and symptoms like angina pectoris, evidently connected with the heart. I saw him, and came to the conclusion that there was something more than mere functional angina (as it is called). I came to the conclusion that there was an organic lesion, and before the death occurred, twenty-four to thirty-six hours later, I thought that there was considerable probability that it might be aneurismal, and I pointed out to the medical attendant the probability that an aneurism might form suddenly under the circumstances in which this gentleman was, and might terminate fatally, suddenly, in something like a dissecting aneurism. That happy hit of mine got for me in the mind of this medical attendant, a most intelligent and highly experienced man, an enormous amount of what we may call κῦδος. He thought, and freely expressed to me his opinion, that it was almost a preternatural sagacity on my part that issued in this diagnosis, when at a post-mortem examination the artery was found in precisely this state. There was a distinctly transverse tear in the inner coat, almost like the cut of a knife

extending about half an inch in one direction; then a dissection of the middle coats for an inch or so opening into the pericardium. I explained to the gentleman that whatever seemed to be preternatural in the diagnosis was in consequence of the way in which the case of this negro in the Chatham museum had stuck during all these long years in my memory. This patient had been a very free liver—given to drinking-bouts, in the midst of one of which he became suddenly very ill. He came home in a dazed condition, and at once complained of his heart, and died about twenty-four hours afterward.

I am rather struck with Dr. Peabody's statement that in attacks of angina pectoris we observe a difference in the two radial pulses. He stated that as an ascertained fact. It is not an ascertained fact in my mind. So far as my reading and personal knowledge of the subject go, I have no cause to believe that there is any difference; unless, indeed, the angina-like symptoms depend, as they may do, upon aneurism.

Dr. Ord's allusions to gout in connection with this subject, and his allusions to the probable differences in America in the field of experience in that matter, leads me to make one further remark. I believe he is quite right there. I believe the experience of London is like the experience of no other place on the face of the earth in regard to gout. I do not think that there is any other place in which there is nearly the same prevalence of gout and all sorts of gouty lesions. In Scotland we are very far from having the same amount of gout as in London, although I have no doubt that it has been increasing in my own time, because of the development of habits, not of drinking, because we drank in Scotland long before, but habits of self-indulgence in connection with indolence. The use of carriages is a great element in gout; people who do not set up carriages do not have gout. In Scotland even the wealthy merchant often walks to his business. There is an expression used in Glasgow which says that "gout came in when Glasgow punch went out." That really amounts to a change in the social status, and in the habits of certain parts of the population. Glasgow punch, although it bore a bad name, was an extremely reasonable drink if taken in anything like moderation. "Glasgow punch" represented a state of society when port, and sherry, and claret were much less used than they are now, and no doubt the change from it to the more luxurious and expensive drinks, together with the other changes in respect to raising the level of apparent social comfort, and the use of the carriage, has brought about in late years a much greater amount of gout than before.

There are other pathological facts connected with the social habits which are more striking to me even than the differences in the amount of gout. One is this—and I state it here because in America you have better means of arriving at conclusions about it than we can possibly have in our little group of islands: When Dr. Ross, of Manchester, and others began to make our minds in Scotland familiar with the subject of peripheral neuritis in its supposed, and apparently recognized, connection with alcoholic drink, alcohol

being recognized by him and many others as being almost the only ascertainable etiological factor in peripheral neuritis, I made the remark that we saw really surprisingly few of these cases in Scotland. Of course, in saying so, I was quite well aware that a man may look at a thing for years and years without knowing it to be there at all, and I was perfectly aware that the disease might have passed under my observation without being noticed. But by a happy accident I was acting as an examiner in the Victoria University in Manchester some years ago, and Dr. Ross took me into the Royal Infirmary there and showed me at once almost a dozen cases of this disease in different stages. I have kept my eyes open ever since, and I have no hesitation in saying that in Scotland (where, I am very sorry to say, we still drink a great deal of whiskey) alcoholic peripheral neuritis is a much more rare disease than it appears to be in Manchester, or probably in London. What is the cause of that? I do not know. It must have a cause, and I think, as I said before, your great congeries of population will afford a great opportunity for its solution.

DR. COUNCILMAN: I will only say that it is not my intention to disparage the work of Drs. Gull and Sutton. I think that their work has not only been the pioneer work, but its actual value deserves the greatest amount of credit. I think they did make some rather slight mistakes, possibly in their histological conception of the process.

I will also say that I regard it as a mistake, in all these cases of arteriosclerosis which we have examined, that we have not looked for a gouty deposit in the great toe.

INTESTINAL PERFORATION IN TYPHOID FEVER: ITS PROGNOSIS AND TREATMENT.

By REGINALD H. FITZ, M.D.,

SHATTUCK PROFESSOR OF PATHOLOGICAL ANATOMY IN HARVARD UNIVERSITY; PHYSICIAN TO THE MASSACHUSETTS GENERAL HOSPITAL.

At the fifth annual meeting of the Association of American Physicians, Dr. Reeves,[1] in his paper on "Typhoid Fever," says:

"I have seen in five instances all the symptoms which announce and follow perforation of the bowels, yet the patients recovered."

During the subsequent discussion, Dr. Loomis[2] stated:

"I do not remember to have seen a single recovery after there were unmistakable evidences of intestinal perforation. Recovery from a local peritonitis complicating typhoid fever is not uncommon, but when the characteristic symptoms of intestinal perforation are present, in my experience, a fatal issue soon follows."

With such a divergence of opinion, so lately expressed, it seems desirable to reinvestigate the subject of intestinal perforation in typhoid fever, with the view of harmonizing conflicting opinions concerning its mortality, and, especially, with the hope of obtaining evidence which might aid in the treatment of this usually, if not invariably, fatal complication.

The frequency of its occurrence has been most recently considered by Schulz,[3] who found that peritonitis from intestinal perforation took

[1] Transactions of Association of American Physicians, 1890, v. 17.

[2] Loc. cit., v. 21.

[3] Centralbl. f. allg. Path. u. path. Anat., 1891, ii. 289. Jahrb. d. Hamb. Staats-Krankenanstalten, 1889, i.

place in 1.2 per cent. of 3686 cases of typhoid fever treated in the Hamburg hospitals during the years 1886 and 1887. He thus essentially confirms the statement of Liebermeister,[1] who found intestinal perforation in 1.3 per cent. of rather more than 2000 typhoid patients in the hospital at Bâle between 1865 and 1872.

As a cause of death in fatal cases of typhoid fever it was found by Hölscher[2] to occur in 6 per cent. of 2000 cases. Murchison[3] found a much greater frequency—11.38 per cent. in 1721 cases collected from various sources. But in 4680 cases of typhoid fever, as tabulated by various authors, I find a mortality of only 6.58 per cent. from this cause, thus practically agreeing with Hölscher.

It occurs much more often in man than in woman. In 444 cases, I find it among men in 71 per cent. and among women in 29 per cent. Its occurrence among children in very rare. Wolberg[4] found no case of intestinal perforation among 277 cases of typhoid children in the Warsaw hospital. The following table, representing a collection of cases chiefly from periodical literature, shows the relative frequency of the occurrence of intestinal perforation in typhoid, at the different periods of life:

AGE AT WHICH PERFORATION OCCURS.

Age.	Cases.	Per cent.
1 to 10 years	7	3.6
10 to 20 "	46	23.8
20 to 30 "	77	39.8
30 to 40 "	45	23.3
40 to 50 "	14	7.2
50 to 60 "	2	1.0
60 to 70 "	1	0.5
	192	

The perforation may take place from the end of the first week to the sixteenth week, as shown by the comparison of symptoms and lesions in 193 cases. The following table illustrates this point:

[1] Ziemssen's Hdb. d. sp. Path. u. Therap., 1874, ii. 1, 161.
[2] Münch. med. Woch., 1891, xxxviii. 64.
[3] Treatise on Continued Fevers, 2d edition, 1873, 566.
[4] Jahrb. f. Kinderheilkunde, 1888, xxvii. 28.

DATE OF OCCURRENCE OF PERFORATION.

Week.	Cases.	Per cent.
First	4	
Second	32	16.5
Third	48	24.8
Fourth	42	21.7
Fifth	27	14.0
Sixth	21	13.4
Seventh	5	
Eighth	3	
Ninth	2	
Tenth	4	
Eleventh	3	
Twelfth	1	
Sixteenth	1	
	193	

The seat of the perforation in 167 cases was the ileum in 136 (81.4 per cent.), the large intestine in 20 (12.9 per cent.), the vermiform appendix in 5, Meckel's diverticulum in 4, and the jejunum in 2. In 19 cases there were two perforations, in 3 there were five, in 1 there were four, and in 4 there were several. In one case[1] there were twenty-five to thirty holes, and in another[2] there were thirty.

The duration of life after the symptoms of perforation arose was usually short. Of 134 cases, 37.3 per cent. died on the first day, 29.5 per cent. on the second day, and 83.4 per cent. during the first week following the onset of the symptoms. During the second week 9 died, 4 during the third week, while 1 lived thirty days and another thirty-eight days.

There is no definite relation between the severity of the individual attack and the occurrence of perforation. In about one-fourth of nearly 200 cases, the course of the disease was distinctly stated as mild. Cases of walking typhoid in which perforation took place were numerous—14 in all. Sévestre[3] reports one under his observation as "of typhoid fever without marked signs till the outbreak of grave symptoms." The case is reported by Bennett[4] of a man who was admitted to St.

[1] Hoffmann: Untersuch. u. d. path. anat. Veränd. d. Organe beim Abd. Typh., 1869.

[2] Lebert: Ueber d. Typhus u. d. Typh. Epid. d. J. 1857. Friedrich: Die Paracentese d. Unterleibs b. Darmperf. im Abd. Typh., 1867.

[3] Bull. Soc. Anat., 1871, xlvi. 360.

[4] Trans. Path. Soc. London, 1866, xvii. 121.

Thomas's Hospital for cardiac disease, with general dropsy. He was purged, and, in consequence of his voracious appetite, was allowed liberal diet, including meat. After a fortnight his bowels became loose for a couple of days. Complaint was then made of general distress. There was some abdominal tenderness, which was thought to be due to peritoneal inflammation from affection of the kidneys. Sudden death took place the next day from typhoid perforation of the ileum. Finucane[1] reports a case as apparently well till within two days of his death, when symptoms of perforation took place. Kleinwächter[2] records a similar case. The patient, a woman, was about her business till forty-eight hours before death, when the symptoms of perforation began.

As the cases of typhoid fever in which intestinal perforation occurs may be mild or severe, so may the symptoms of perforation be absent or latent, gradual or sudden. Of 80 cases in which a record is made of these characteristics, it was found that in 56 the onset of the symptoms was sudden, in 15 cases the symptoms were gradual or latent, while in 5 there were no symptoms whatever of perforation.

Laboulbène[3] reports two cases of peritonitis in typhoid fever from perforation discovered after death:

"Not having during life the ordinary and characteristic symptoms . . . there was neither severe pain, vomiting, nor tympany. The only signs which attracted my attention and which made me think of the possibility of intestinal hemorrhage, was a lowering of the axillary temperature with considerable chilliness of the skin."

Barth[4] had a somewhat similar experience. He says:

"It was impossible, despite the closest watching, to determine with certainty the moment of perforation; the patient had neither violent abdominal pain, vomiting, nor collapse, and only the somewhat sudden lowering of the temperature, on the morning of the 9th of February, led us to suppose, afterward, that the onset of the disturbance then took place."

Jenner[5] reports the case of a patient who, on the ninth day, left his bed unassisted, but with some difficulty, and died some hours later, there being no complaint of pain during the day.

[1] Lancet, 1889, ii. 793.
[2] Wiener med. Presse, 1880, xxi. 337.
[3] L'Union Médicale, 1877, xxiii. 389.
[4] Bull. Soc. Anat., 1884, lix. 142.
[5] Medical Times, 1850, xxii. 298.

Differences of opinion concerning the fatality of intestinal perforation in typhoid fever have existed for many years. The earlier investigators, as Louis,[1] Chomel,[2] and Jenner,[3] reported numerous cases of fatal perforation, but none of recovery. Tweedie[4] stated that "intestinal perforation is always fatal, generally within thirty-six hours." The possibility of recovery seems to have been first suggested in the case reported by Buhl,[5] who states that

"One of the cases of perforative peritonitis was interesting because death was not the immediate result of the perforation, since the hole was completely closed. Death occurred on the forty-fifth day of the disease and twenty-three days after the earliest symptom of perforation. It was the result of hemorrhage from a small artery opening into the intestine near the piece of mesentery which covered the hole."

Griesinger,[6] after referring to the above case, and giving the history of one of his patients who died nine days after symptoms of perforation had taken place, admitted the possibility of the healing of a perforation and of recovery:

"never in cases of general peritonitis, only when the inflammation is wholly circumscribed. The rare exceptions are hardly worth considering in connection with the prognosis, which is to be regarded as almost fatal when the symptoms of perforation are distinct and as absolutely fatal when gas is present over the liver."

A somewhat more favorable opinion was held by Murchison,[7] who asserted that "rare cases are met with where recovery ensues after all the symptoms of peritonitis from perforation." Since the publication of Murchison's classical work the writers of medical text-books have generally held the same opinion, and medical literature contains occasional reports of cases of recovery. It is our task, therefore, to consider the evidence which warrants the view that recovery ever takes place.

The evidence of recovery from intestinal perforation in typhoid fever consists, almost exclusively, in the reports of cases of recovery

[1] Recherches sur la Maladie connue sous les noms de Gastro-entérite, etc., 1829.
[2] Leçons de Clin. Méd., 1834.
[3] Monthly Journal of Medical Science, 1849.
[4] Cycl. of Pract. Med., art. "Fever," 1850, ii., 162.
[5] Zeitschr. f. rat. Med., 1857, N. F., viii. 12.
[6] Virchow's Handb. d. sp. Path. u. Therap., 1864, ii. 1, 199.
[7] Op. cit, 569.

from peritonitis in typhoid fever following so-called symptoms of perforation of the intestine. These symptoms are, in brief, a sudden, severe abdominal pain, often associated with collapse, at times with a lowered temperature, which is subsequently elevated. The abdomen is rigid and tender, and becomes swollen, tense, and tympanitic. But little importance is to be attached to the disappearance of hepatic dulness and to the presence of a gurgling sound on respiration as evidence of gas in the peritoneal cavity in consequence of a perforated intestine. The former sign may be due to an abnormally small liver or to an overlying piece of intestine, and the dulness is usually found to persist when the intestine is actually shown to be perforated. Traube,[1] in calling attention to this sign, stated the importance of the previous determination of the normal outlines of the liver dulness. Tschudnowsky's[2] observation of an abdominal murmur, louder and longer on inspiration, shorter and feebler on expiration, attributed to the passage of gas in and out of the hole in the bowel, has been confirmed by Lewaschow.[3] Botkin,[4] however, states that this sign may exist without perforation of the intestine. The rarity of the recognition of either of these signs in the literature of intestinal perforation is sufficient evidence of their slight value, while the conditions of their occurrence, perforation with the considerable free discharge of intestinal gas, is comparatively infrequent.

The so-called symptoms of perforation merely indicate the beginning of a peritonitis, and may be present as the result of other local causes of peritonitis in typhoid fever than a perforative enteritis. Very rare, though possible, are the various causes of acute intestinal obstruction. Murchison[5] mentions softened infarctions of the spleen, softened mesenteric glands, abscesses in the wall of the urinary bladder, ovarian abscesses, "the bursting inward of a pseudo-abscess in the sheath of the rectus muscle," and, finally, perforating ulcers of the gall-bladder. Rupture of the spleen may be added, as in the case reported by Kiemann,[6] which gave rise to no symptoms suggesting rupture or peri-

[1] Berl. klin. Woch., 1866, iii. 68.
[2] Virchow u. Hirsch, Jahresb., 1869, ii. 133.
[3] Vratch, 1890, No. 3; Centralbl. f. klin. Med., 1891, xii. 270.
[4] Louis. Prog. Med., 1890, xii. 512.
[5] Op. cit., 564.
[6] Ber. d. k. k. Krankenanstalt. Rud-stift in Wien v. J. 1888, 1889, 291.

tonitis. Sorel[1] reports a case of subacute peritonitis the result of an abscess of the liver. A like cause gave rise to a rapidly fatal peritonitis in the case reported by Daly.[2]

Still another source of acute peritonitis in typhoid fever is to be found in the Fallopian tube, as in the case reported by Wilson.[3] His patient, a child of twelve years, died thirty-six hours after the sudden onset of abdominal pain, which was attributed to a salpingitis of the left Fallopian tube, found at the post-mortem examination. Beginning ulceration of Peyer's patches was present in the lower part of the ileum. Ranque[4] credits Bourdon with a case which may have been of a like nature. The patient was nineteen years old. After several days of prolonged symptoms she was seized with abdominal pain, a violent chill, and suppression of the catamenia. Death took place six days later. There were beginning typhoid ulcers, but no perforation. The same author refers to Jaccoud as reporting a case of peritonitis in typhoid fever from rupture of the urinary bladder.

Still another cause of peritonitis in typhoid fever is illustrated in the case reported by Hoffmann.[5] The patient gave birth to a child during the course of the fever, and died of diphtheritic endometritis and general peritonitis.

It is unnecessary to call attention to the numerous fatal cases of peritonitis in typhoid fever in which no local cause for the peritonitis was found. Jenner[6] early published an article on the "Symptoms of Perforation of the Intestine without Existence of that Lesion." Of the case observed by him he says: "All the symptoms said to denote the occurrence of perforation of the intestine were also present, but in her case an examination of the body after death found those symptoms might be present without any traumatic lesion of the peritoneum." Wood,[7] a few years later, thus remarks:

"I was compelled, therefore, to regard the case as one of peritonitis without perforation. No discoverable cause of the affection existed. . . . This case is calculated to throw great doubt upon the existence of intestinal perforation in those instances of peritonitis occurring in the advanced stage of

[1] L'Union Méd., 1882, xxxiv. 521.
[2] Philadelphia Med. and Surg. Rep., 1882, xlvi. 346.
[3] Arch. of Pediat., 1887, iv. 391.
[4] Thèse. Paris, 1881.
[5] Op. cit.
[6] Med. Times, 1850, xxii. 405.
[7] Trans. Coll. Phys., Philadelphia, 1853–6, ii. 351.

typhoid fever in which cures have been effected, of which I have been so fortunate as to witness two in my own experience. They may have been, as in the case just related, nothing more than simple peritonitis without any opening whatever through the coats of the bowel."

Since perforation of the intestine in typhoid fever may take place without any suggestive symptoms, and since suggestive—even so-called characteristic—symptoms may occur without any perforation having taken place, it must be admitted that recovery from such symptoms is no satisfactory evidence of recovery from perforation.

There remains for consideration another set of cases, several in number, of recovery from peritonitis of sudden onset in typhoid fever following the discharge of pus, offensive or not, by the rectum, vagina, or abdominal wall. Food may be present in such pus. Such state-statements of fact do not necessarily show a primary perforation of the intestine, for the latter may have been caused by the peritonitis, which, in its turn, may have owed its origin to some cause apart from an intestinal lesion. One of the most marked cases of this sort is that reported by Low.[1] The patient, five years old, during the course of his fever, developed a hard, painful swelling at the right of the navel, which burst. Offensive pus was discharged, in which were several orange-colored masses as large as beans. The abscess healed ten days later. To accept this case as evidence of recovery from a typhoid perforation of the bowel, it is necessary to assume, first, that the case was one of typhoid fever, and then that there was a communication with the bowel. Of equal, if not of greater, importance in determining the possibility of recovery after typhoid perforation of the intestine, are the cases of prolonged life after the occurrence of symptoms suggesting a perforation with the discovery of the latter after death. Buhl's[2] case has already been referred to. Hoffmann[3] records the case of a man in whom a bilateral pleurisy arose during the course of typhoid fever, at a time when the abdomen was tense, hard, and occasionally painful. Death took place after an illness of some seven months. Toward the end of this time an abscess pointed in the ileo-cæcal region, and was opened. Fecal pus eventually escaped. At the post-mortem examination it was found that the ileum was perfor-

[1] British Medical Journal, 1881, ii. 122.
[2] Zeitschr. f. rat. Med., 1857, N. F., viii. 12.
[3] Virchow's Arch., 1868, xlii. 227.

ated and adherent to the abdominal wall. It opened into an extra-peritoneal fistula, which was continued downward into the groin, where it opened externally, and upward through the diaphragm beneath the pleura. Intestinal contents were thus present in the thorax, but not in the pleural cavity.

The similarity of the symptoms of typhoid perforation of the bowel and those of inflammation of the vermiform appendix is striking. Cases of perforating appendicitis have repeatedly been regarded as of typhoid fever, and, as a rule, the symptoms in typhoid fever which suggest a perforation of the bowel are those which, in the absence of typhoid fever, would be regarded as diagnostic of an appendicitis. These symptoms are not merely similar, they are actually identical, even to the usual localization of the consequent peritonitis in the right iliac fossa. However familiar this resemblance may now appear, the only conspicuous mention it has received in medical literature is by Gouronnec.[1] To be sure, he uses the terms typhlitis and perityphlitis without appreciating the prominent part played by the appendix in etiology, and the cases he reports make no mention of the condition of this structure. He[2] "speaks only of ordinary typhlitis occurring in the course of typhoid fever." The tumor is regarded as feces accumulated in the cæcum in consequence of inflammation of the cæcum. He[3] states that "in many cases the progress of the inflammation of the pericæcal tissue is simultaneous with that of the cæcum, but a pericæcal abscess may sometimes be seen in the absence of an appreciable ulcer of the cæcum."

Despite this extraordinary resemblance between the symptoms of so-called typhoid perforation of the intestine and those of perforating appendicitis, in a research made several years ago I was enabled to find but three cases of this lesion attributable to typhoid fever. It is well known that the mucous membrane of the appendix contains numerous lymph-follicles, and that in typhoid fever these may become enlarged, necrotic, and ulcerated. It is, therefore, noteworthy that but few cases of perforation of the vermiform appendix are recorded in the literature of typhoid fever. Morin[4] finds 12 cases in 64 = 18.75 per cent., which he collected from various sources, while

[1] De la Typhlite et Périty phlite dans leurs Rapports avec la Fièvre Typhoide. Thèse. Paris, 1881.

[2] Loc. cit., p. 9. [3] Loc. cit., p. 12. [4] Thèse. Paris, 1869.

Murchison[1] finds it but once in 39 cases. He suggests a doubt as to the nature of the disease in Morin's cases, in consequence of the large number of perforated appendices. Heschl,[2] among 56 cases, finds the appendix perforated in 8 = 14.3 per cent. But of 167 cases of perforated bowel in typhoid fever, collected for the purposes of this paper, I find but 5 cases, a fraction less than 3 per cent., in which the appendix was reported as the seat of the perforation. Such differences may be explained, as suggested by Murchison, on the ground of an incorrect diagnosis during life. But they are quite as likely to be due to overlooking the appendix at the time of the autopsy. Even in the cases of the fatal peritonitis in typhoid fever, in which it is stated that no perforation was found, there is no mention of the condition of the appendix.

Recent anatomical evidence is thus lacking of a relatively frequent perforation of the appendix in typhoid fever. Clinical evidence, on the contrary, though perhaps misunderstood, is abundant as to the probable frequency of perforative appendicitis in typhoid fever. The probability of its occurrence furnishes the best solution to the prognosis of intestinal perforation in the latter disease. Most cases of recovery from symptoms of perforation of the bowel in typhoid fever are those in which an attack of appendicitis is closest simulated. While the fatal cases of perforation of the bowel in typhoid fever are, in the great majority of instances, those in which other parts of the bowel than the appendix are the seat of perforation. Hence the prognosis of apparent perforation of the bowel in typhoid fever is to be regarded as the more favorable the more closely the symptoms and course resemble those of an appendicitis.

Such a consideration at once indicates the appropriate treatment for perforation of the intestine in typhoid fever. All indubitable cases of this nature were those in which a post-mortem examination was necessary to make the diagnosis certain. The suggestion of a laparotomy for the relief of a perforated bowel was first made by Leyden[3] in 1884. In the same year Mikulicz[4] reports a successful case of laparotomy and intestinal suture in a patient with ichorous,

[1] Op. cit., 623.
[2] Schmidt's Jahrb., 1853, lxxx. 42. Wiener Zeitschr., 1853, ix. 6.
[3] Deutsche med. Woch., 1884, xvii.
[4] Volkmann's Samml. klin. Vortr., No. 262.

purulent peritonitis, attributed to a typhoid, perforating ulcer of the small intestine. The patient had a small, right inguinal hernia, but thought himself well. He was suddenly seized with a violent pain in the abdomen on leaping out of bed. Symptoms of peritonitis ensued, and at the end of the third day laparotomy was performed for the relief of a supposed intestinal obstruction. A median incision was made, offensive pus, in which were pieces of potato, was evacuated, and a hole was found in that part of the ileum lying above the ilium. The hole was opposite the mesenteric attachment, and was six millimetres long and four millimetres wide. Its edges were sharp, the mucous membrane not everted, and there was nothing abnormal in its vicinity except an increased redness of the intestine. The mesenteric glands were soft and about the size of hazel-nuts. Mickulicz excluded the idea of a gangrenous incarcerated hernia, because the outline of the hole was regular and oval; there were no phenomena of a reactive inflammation in its vicinity, and there was no positive evidence in favor of such a view. He claimed that the seat, size, and absence of other characteristic symptoms excluded nearly all other than typhoid ulcers; while its position, edges, and the enlarged lymph-glands were evidence in favor of a typhoid ulcer. Although admitting the force of his argument, there remains a question as to the existence of typhoid fever in this case. Its chief value lies rather in its being a successful case of laparotomy, where a perforation of the ileum away from the mesenteric attachment existed, than as illustrating the value of laparotomy in the treatment of intestinal perforation in typhoid fever.

The first operation for the relief of the symptoms caused by a perforating, typhoid ulcer of the intestine where there is no question as to the nature and seat of the lesion, was performed in 1887, by Lücke.[1] The symptoms suggestive of perforation took place on the eighteenth day of the disease, and a laparotomy was performed twelve hours after their onset. The edges of the ulcer were cut out and the hole closed by sutures. The operation lasted some two hours, and the patient died a few hours later. The hole in the ileum was about a foot and a half above the valve.

In the same year Bontecou[2] operated upon a case of typhoid per-

[1] Deutsche Zeitschr. f. Chir., 1887, xxv. 1.

[2] Journal American Medical Association, 1890, xiv. 455.

foration thirty-six hours after the onset of its symptoms. The patient died. Morton[1] states that Mr. Bartleet, of Birmingham, had performed a laparotomy in the case of a perforating, typhoid ulcer. Death took place two days after the operation. Although feces were found in the peritoneal cavity the hole in the intestine was not discovered, nor is the evidence furnished that the case was one of typhoid fever.

At the meeting of the German Surgical Congress in 1888, Frank[2] stated that Hahn had operated on two cases of peritonitis from perforation in typhoid fever, but both patients died. Fürbringer[3] also refers to the fact of Hahn's operations on some of his patients, all of whom quickly died after the operation. He alludes to the successful operation by Wagner. The fullest mention of this case I have been able to find is as follows:[4] "Wagner (Kŏnigshutte) in recent years, has operated in three cases; first, on a woman convalescing from typhoid fever, for perforation of an intestinal ulcer; eventration of the intestines, irrigation, sutures of the wound without drainage. Recovery."

In 1889, Senn[5] operated upon a patient who was thought to have a volvulus. He had been treated for chronic bronchitis for three weeks, during which time he had made three visits to Dr. Senn's office. The temperature was never above 101° F. At the end of the third week there was an acute attack of pain in the left iliac region, followed by vomiting which became stercoraceous. Laparotomy was performed at the end of three days. "A number of loops of the upper portion of the ileum were found enlarged twice the size of the remaining portion of distended intestine, rotated on the mesenteric axis one complete turn from left to right." While the over-distended intestine below this point was being withdrawn, about a pint of fluid feces gushed from the left iliac fossa. Perforation was discovered about six inches above the ileo-cæcal valve. The hole was closed by sutures. The operation lasted an hour, and death took place in the course of a few hours. Three elliptical ulcers of the ileum were found below the point of perforation.

[1] Philadelphia Medical News, 1887, li. 617.
[2] Beil. zum Centralbl. f. Chir., 1888, xxiv. 51.
[3] Berl. klin. Woch., 1889, xxvi. 667.
[4] Beil. zum Centralbl. f. Chir., 1889, xxix. 66.
[5] Medical News, 1889, liv. 622.

Bontecou[1] operated upon a patient who was in the sixth week of typhoid fever. Seventeen hours after the onset of symptoms of perforation a circular hole about one-fifth of an inch in diameter was found in a patch some four or five inches from the ileo-cæcal valve. The hole was closed with sutures, but the patient died after a few hours.

In the *British Medical Journal*[2] is the following extract from a Japanese medical journal:

"Kimura, a surgeon in the Japanese navy, records a case in which he performed laparotomy for perforating typhoid ulcer. The patient was a man aged thirty-four. The operation was done twenty-eight hours after the occurrence of perforation, when the patient was collapsed and almost moribund. The perforation in the small intestine, about two inches above the cæcum, was of the size of a small pea. The perforated part of the intestine was turned inward, and ten interrupted Lembert sutures applied. The abdominal cavity was washed out with a warm solution of dilute boric acid and dried with a sponge; a large gum-elastic tube was introduced, and the wound stitched up and dressed antiseptically. The patient was 'cheerful' for a little time, but died about nine hours and a half after the operation."

Early laparotomy in typhoid perforation of the intestine (with a reasonable doubt as to the existence of typhoid fever in three of the cases) is thus recorded to have been performed ten times. The result was fatal in every case but one, that of Wagner, a complete record of which does not appear to have been published. The inference is direct that this operation offers but slight hope in the early stages of typhoid perforation of the intestine. A like result occurs when the perforated spot is quickly found, as when a couple of hours are demanded for the operation. The lack of success is best attributed to the condition of the patient at the time enfeebled, as he usually is between the second and fourth weeks of the disease, when the perforation is most likely to take place.

Fatal as the results of this early operation have been in cases of peritonitis from typhoid perforation of the intestine, they have been more successful when a peritoneal abscess has been incised some time after symptoms of suspected perforation have taken place.

Barthélemy[3] records the case of a young soldier, who, at the end of

[1] Loc. cit. [2] British Medical Journal, 1890, ii. 777.
[3] Ann. d. Chir. franc. et étrang., 1841; Gouronnec, op. cit.

typhoid fever, had a severe, deep-seated pain in the right buttock, extending to the kidney. An abscess was recognized in the iliac and lumbar regions. An opening was made a little above the iliac crest and three litres of pus escaped. The patient recovered.

Escher[1] reports as a case of recovery from supposed intestinal perforation in walking typhoid, one where an abdominal incision was made for the relief of a suspected incarcerated right inguinal hernia after the third day of abdominal symptoms.

Taylor[2] states that a relapse took place in a patient thought to be convalescing from a severe attack of typhoid fever. The symptoms were more acute and dangerous than at first, and, at one time, there was so much collapse that a perforation was suspected. A tumor then formed between the sternum and navel, and was incised four months after the disease began. Three pints of brown, slightly turbid fluid were evacuated. The patient recovered.

Although the reported instances of the successful result of an operation for the cure of circumscribed peritonitis in typhoid fever are comparatively few, I have been able to collect a considerable number in which recovery resulted from resolution or from the spontaneous evacuation of the inflammatory product. In 17 cases of recovery by resolution, the peritonitic attack began in the second week in 1, in the third week in 8, in the fourth week in 1, in the fifth week in 1, and in the sixth week in 2. It began at the end of the fever in 1, and during the convalescence in 3. Recovery took place in a week in 1, in two weeks in 3, in three weeks in 2, in four weeks in 1, and in two or three months in 3. The length of time necessary for recovery in the remaining cases was not stated.

I find also 17 cases of the spontaneous discharge of the pus in peritonitis in typhoid fever. 9 patients recovered, 7 died, while in 1 case the result was not stated. The peritonitic symptoms began in the second week in 2 cases, in the third week in 3, in the fourth week in 2; in 1 walking case, in 6 convalescent cases, and in 3 during the course of the disease. Death is said to have taken place in six, fourteen, and fifteen days, in three weeks, and in two and one-half months after the symptoms began. The pus was discharged into the intestines

[1] Wiener med. Woch., 1887, xxxviii. 607.
[2] Lancet, 1890, i. 961.

in 13 cases; into the vagina in 1, through the abdominal wall in 2, and at the navel in 1.

It appears from this statement that of 27 cases of peritonitis in typhoid fever, whatever may have been the cause of the former, though often attributed to intestinal perforation, 3 recovered after operation, 17 after resolution, and 9 after the spontaneous discharge of the pus. The comparison of this series of cases with those showing the results of early laparotomy for symptoms suggesting typhoid perforation indicates that the appropriate treatment for this complication would be delay until a probably encapsulated exudation proved unduly slow in absorption. An immediate or early laparotomy for the relief of the peritonitis seems advisable only when the patient's condition is exceptionally good. Should the signs of the exudation persist a week or more, and the general condition of the patient permit an incision, surgical treatment would then be strongly advisable. That the patient may live for weeks after perforation has taken place is illustrated by the cases of Buhl and Hoffmann already mentioned.

In brief, immediate laparotomy for the relief of suspected intestinal perforation in typhoid fever is only to be advised in the milder cases of this disease. In all others, evidence of a circumscribed peritonitis is to be awaited, and may be expected in the course of a few days. Surgical relief to this condition should then be urged as soon as the strength of the patient will warrant.

DISCUSSION.

DR. DA COSTA: The paper just read is of the thorough and lucid character which we always associate with the writings of Dr. Fitz. The paper, so suggestive, makes one of two points, it seems to me, clear. First, that whenever we have perforation of the bowel in typhoid fever, and look to any therapeutic procedure, we ought to endeavor to ascertain accurately where the perforation is. Is it in the appendix, or in the bowel itself? I have nothing to add to what has been said with reference to this extremely interesting suggestion, but as regards perforation and an operation for its relief, it so happens that I have some personal knowledge. I am cognizant of cases in which the operation was performed—one of them was operated upon within eighteen hours after the perforation. The case was this: A young man, twenty years of age, had typhoid fever of not severe type. The fever was nearing its termination at the end of the third week, and the temperature

was scarcely above the normal; everything pointed to speedy convalescence. Presuming on his recovery, the young man ate, when not watched, a hearty meal, chiefly of meat, and a few hours afterward was seized with violent pain in the neighborhood of the right iliac fossa, and soon signs of collapse came on. The family physician, Dr. Steinbach, who had seen him at half-past one in the day doing perfectly well, found him shortly after six o'clock in the afternoon with evident signs of perforation; he had had a violent chill. Early next morning an operation was determined upon, as the only thing giving him a chance, and was urged by the patient himself, whose mind had remained perfectly clear. The temperature before the operation was 104.5°. Laparotomy was most skilfully performed by Dr. Morton; the perforation was found in the small intestine, about three feet above the ileo-cæcal valve, and the lesion repaired, but the young man, conscious almost to the last, and free from pain, died during the night.[1] At the autopsy only a very slight amount of peritonitis was discovered; a few of the intestinal coils were adherent by a small amount of healthy-looking lymph; the peritoneum everywhere else was absolutely clean, and free from exudation, pus, or blood.

In another case of which I have cognizance, I know less of the details. The operation was performed in the last stages of typhoid fever for intestinal perforation; but it was not done as soon as in the preceding case; it was not successful. The seat of lesion was, I think, in the small intestine, some distance above the ileo-cæcal valve.

My knowledge of these cases, and the results in the published ones I have examined, has not made me think favorably of laparotomy in typhoid fever. Indeed, I may say that, with my present information, I would not counsel an operation in perforation, unless I could make out an appendicitis as the cause of the rupture, or unless the operation were performed for the relief of the patient, free from the consequences of a subsequent peritonitis.

[1] Details of the case and particulars of the operation are described by Dr. Morton in the Medical News, December 24, 1887.

THE RELATIONS OF DRINKING-WATER TO DISEASE.

By HENRY P. WALCOTT, M.D.,
CAMBRIDGE, MASS.

THE vast literature upon the subject of drinking-water and its influence upon human health contains but little that is of real value to the physician in helping him to cure or to prevent disease.

Outbreaks of epidemic disease have, indeed, often been believed, by people and physicians, to be the result of some unknown pollution of a water-supply, possibly by the intentional addition of a poison. The plague that fell upon the Athenians at the time of the siege of their city by the Peloponnesians, the inevitable companion of crowding, bad food, and neglect, was attributed by the besieged to a poisoning of the wells by the enemy. In all times, down to our own even, the common people have returned to this idea of a poisoning of the water-supply whenever an epidemic disease of unusual severity has been prevalent.

The correct appreciation of the influence of drinking-water in the production of disease may be said to date only from a time within this half-century. The peculiar distribution of Asiatic cholera in London, in the epidemics of 1848–49 and 1853–54, attracted the attention of Dr. Snow and others; evidence was brought forward to show that certain waters, obviously contaminated by human waste, had some very direct relations to the spread of this disease. The conclusions arrived at by Snow were not accepted by the profession with anything like general assent, and there still is a very influential body of observers who assign to drinking-water a quite subordinate place in the production of disease. At this time began a more careful examination of water and its pollutions; at first by means of chemistry only, through the help of which it was hoped that certain standards of purity might be established; an attempt not yet abandoned. The difficul-

ties in the way of creating such standards seem, however, to be nearly insurmountable.

The bare statement from the chemical laboratory of the constituents of a water submitted to analysis conveys but little information. The amounts of the various substances contained in even the worst waters used for public supplies are almost insignificant in quantity, and the chemical combinations enumerated appear to be, in themselves, innocuous.

When to these considerations is added the fact that of two waters, one capable of producing serious disease and the other not, the first may be found to contain less of substances open to suspicion than the second, it is not much to be wondered at that even the trained physician should lose faith in the immediate value of water analysis.

The chemical examinations of waters, when epidemics prevailed, revealed undoubted pollutions; but, so far as chemistry was relied upon as proof, the pollutions were often no greater during an epidemic of infectious disease than they had been before it, and no less than they would be when the epidemic was past.

Improvements in the methods of determining both the kinds and the number of the minutest forms of organic life, and the proved connection of some of these forms with infectious diseases, have given to us more satisfactory means for the proof of the harmfulness of certain waters than chemical analysis has hitherto afforded.

The careful observer soon realized that there were certain considerations always to be retained in mind when studying the question of water-supplies:

1. There can exist no really pure water in nature.

2. The impurities revealed by chemistry in waters are not necessarily injurious, and, even when they are harmful, vary much in their importance; this variation being determined largely by the origin of the water.

3. There may be every clinical evidence that a given water is injurious to health, and yet chemistry fail to detect the dangerous element. There may be no clinical evidence of such injury, and still the water be found to be polluted in a serious degree, and in a manner always fraught with danger.

4. A number of well-ascertained diseases of man are now known to

be produced by microscopic organisms which are capable of living in water, and have thus far not been detected therein by chemistry.

The beginning of a satisfactory knowledge of the relation of water to health must be made, then, with the most complete study possible of all that natural waters may and do contain; of all the conditions, at all seasons and places, which may affect water, not only in a state of nature, but also under the influence of the changes caused by the presence of human life. Such an investigation had not been undertaken until quite recently.

Chemical analyses had indeed been made for many successive years of a limited number of water-supplies, generally those of large cities; but they had not been accompanied by biological studies, and the interpretations of the results of the analyses had been formulated by the chemist in his laboratory with but little, if any, acquaintance with even the physical conditions which might affect the water.

In the year 1886 the Commonwealth of Massachusetts enacted certain laws to protect the purity of inland waters, and placed the oversight of the water-supplies of the State in the control of the State Board of Health Liberal appropriations of money have also been made from time to time to enable the board to study thoroughly the inland waters of the State, and to conduct such experiments and investigations as might seem advisable. All the resources of the most advanced laboratory methods of to-day have been united to an extended study of the physical condition and environment of the waters. It was held to be indispensable that an accurate knowledge should first be obtained of the natural history of the various waters; to gain this information bodies of water were examined which are not now used for domestic purposes, and, in their present state, cannot be so used. Experiments have been made at a carefully arranged experiment station at Lawrence for the purpose of studying the various methods by which water and sewage may be purified, either under natural conditions or by artificial contrivance. The following remarks are founded mainly upon the results of these investigations, and the facts to sustain the conclusions hereafter stated are to be found in the reports of the Massachusetts State Board of Health, either already or soon to be in print.

Massachusetts contains 25 cities and 326 towns. All the cities and 107 of the towns, or 132 municipalities in all, are wholly or in part

provided with public water-supplies. The population of the places supplied is 1,600,000, or 83 per cent. of the total population of the State. The water is drawn from 128 distinct public sources, divided into 54 which furnish ground water and 74 surface water. Less than one-sixth of the public water-supplies were in existence before the year 1870.

The physical, chemical and biological examinations which have been made have fully met the expectations formed as to their value, and have also shown that observations covering short periods of time not only did not disclose the real character of the water, but might actually mislead. In studying these thousands of analyses of widely differing waters, together with the results of the experimental work of the station at Lawrence, we have been compelled to give up all former standards of purity based upon the organic nitrogen, ammonia, nitrates and nitrites; because these substances, in the quantities that are ever found in natural waters, cannot of themselves be harmful, and no one of them, considered alone, can be convicted of dangerous origin.

With out present information we must assume that the real danger lies in the presence of microscopic organic life or the products of that life, and the essential value of the chemical analysis is to be found in the information given as to this contamination by living organisms.

When water sources are openly exposed we rarely need the services of a chemist or biologist to inform us whether there is pollution or not; our own senses can discover it; but chemistry can tell us much as to the amount and state of the polluting substances. In the case of ground waters the conditions of the investigation are different; here water moves through unseen channels and is subject to certain changes in the nature of filtration, using the word in its widest significance, which cannot be detected except by help of chemistry.

There are many ways in which a water may produce disturbances in the human system.

The human parasites which are known to occur in surface waters are numerous, and may enter the body fully developed or in the form of ova. They are easily found in the water by the use of the microscope, and can be readily removed by filtration or destroyed by the application of sufficient heat. Inasmuch as the moment of entrance into the system can never be accurately fixed, it is almost impossible

to trace the source of any individual infection to a special water. The possibility of this danger requires, in addition to the bacteriological and chemical examinations, the use of the microscope; though adequate protection cannot rightfully be expected from this infinitely limited means of inspection.

Waters may contain substances which, either by quality or by mere quantity only, disturb the system. The well-known action of some of the mineral contents of natural water may be cited. Large quantities of vegetable matter appear oftentimes to be injurious, either by the direct action of some toxic element or by reason of the products of decay.

Bacteria, in their varied forms of vital activity, are associated with all the changes of organic matter in nature, either in the way of decay or oxidation. Very few of the species of bacteria found in water have been proved to be harmful when taken into the human stomach. It is, however, not improbable that the products of their vital processes may be injurious, by reason of quantity, when these organisms exist in vast numbers. There are, moreover, the disease-producing bacteria, limited in number, undoubtedly associated with the harmless varieties, found in the excreta of the sick, and mingled with the waste products of human life, gaining access to bodies of water which are used as sources of supply. In our present lack of accurate knowledge, we may also assume that certain bacteria, which are not in the line of descent from those which have ever been present in a diseased human body, may, upon gaining entrance to it, become the cause of disease.

The doctrine that the contamination of water by the products of human life was dangerous to health had the sanction of divine authority among the higher races of antiquity. A provision of Roman law, from the earlier days of the republic, punished him who polluted a water-supply.

The belief in the necessity of a pure water-supply led to the construction of some of the most enduring monuments of antiquity.

In the absence of a system for the removal of sewage, or in the presence of a system faultily constructed, the pollution of the soil goes on at a rate which keeps the increase of the human race in check.

The microörganisms of disease offer the simplest explanation of the

harmful qualities of the drainage which contains the excreta of the sick. As the senses of sight, smell, and taste offer us no protection against the waters that contain any of the now known disease-producing bacteria, we must seek for safety in the case of waters which are known to be unpolluted by sewage, or, if this be impracticable, waters which, though sometimes polluted, have been rendered harmless.

It has been ascertained that the sewage of a manufacturing city, abundantly supplied with water from a public supply, contains less than one-tenth of 1 per cent. of foreign matter, which is, for the main part, inert mineral substance.

One-twentieth of 1 per cent. only of the sewage itself is made up of organic matter and the products of its changes. The dangers and the offensive qualities of the mixture reside in this small amount of material capable of decomposition. By studying this process of decomposition, it is found that recent pollution of water is characterized by the presence of ammonia and the nitrites; a more advanced stage by the formation of the nitrates.

A radical difference between surface water and soil water must be constantly borne in mind. In the former, organic matter, changed by processes of oxidation, becomes a food capable of being appropriated by animal and vegetable organisms. In the ground water, however, though the bacteria present in the upper layers of the soil have a marvellous capacity for reducing organic matter, there is not found here the organic life to appropriate the food; and this passes into the subsoil water or flows away in subterranean channels, and, whenever exposed again to light and air, helps to the formation of organic nitrogen by promoting organic life.

No better classification of waters, from a sanitary point of view, can at present be made than the division of them into two classes: the first, to consist of the waters polluted to a greater or less degree by the waste of human life; the second, those not so polluted. The normal or natural waters may or may not be acceptable to the palate; they may be highly colored; they may even, with the limitations of our present knowledge, be suspected of serving as the carriers of the infection of malarial diseases; but they have not been contaminated by man.

Chemistry alone does not suffice to distinguish, except in extreme

cases, a normal surface water from one contaminated by sewage. Every one of the nitrogenous compounds may be found in greater quantity in some natural water than in one known to be polluted by sewage. A diligent examination of the surroundings will hardly fail to throw sufficient light to clear away the doubt.

Fortunately one element, everywhere accompanying human waste, appears in sewage and survives all the changes that this mixture undergoes—chlorine, the representative of common salt.

From a very large number of determinations of the chlorine present in the waters of Massachusetts, it is apparent that there is a progressive increase in amount from the western border of the State to the seaboard.

Advantage has been taken of these determinations to construct a chart upon which are drawn certain lines of equal chlorine contents of normal waters, or "isochlors." These lines have a general parallelism with the coast line. They have stood the test of repeated trials and full reliance is placed upon them in all cases, except of wells very near the seacoast. The chlorine in the waters known to be nearly or quite free from human contamination varies from 0.06 of 1 per cent. in parts per 100,000, in the extreme northwestern corner of the State, up to an average of more than 2 per cent. per 100,000 parts, on the island of Nantucket and portions of Cape Cod.

When a water brought in for analysis shows an amount of chlorine greater than that designated by the "isochlor" of the locality, the presumption of pollution by sewage, more or less remote, is seldom a mistake. It must not be inferred that this chlorine represents a direct addition of sewage to the water under examination. It has a far more important significance, for it stands in immediate relation to the number of people living on the drainage area, above the point at which the sample was taken; whether the district have sewers or not, provided always that the sewage is not carried beyond the district.

We have no data yet sufficiently complete to enable us to determine precisely the amount of chlorine added by each inhabitant per day to the sewage of his district. Our observations, however, enable us to say, in a general way, that four families or twenty persons per square mile will add on an average, 0.01 of a part per 100,000 of chlorine to the water flowing from the area in question.

The organic matters have not this unchanged character. When sew-

age enters a stream by a direct channel, the water shows the presence of decomposing organic matter; if the waste matters only reach the stream after passage through the soil they may have become completely oxidized, and there will be nothing left to tell the story of previous pollution with any useful degree of certainty, except the unchanged chlorine.

The conditions of nitrogen that have usually been determined in surface waters are: albuminoid ammonia, ammonia, nitrates, and nitrites; these indicate the quantity, kind, and state of the organic matter in the sample.

The albuminoid ammonia does not by itself give any information as to the character of the organic matter contained in the water. Attempts to distinguish between animal and vegetable matter, by means of the relative proportions of the carbon to the nitrogen, have had but a limited success. An examination of the locality generally gives the answer to this question. The tendency to decay of organic substances can be detected by successive analyses of portions of the same specimen and the rate of the changes ascertained. It has thus been discovered that many of the waters containing organic material have a very slight tendency to decay. This statement has especial reference to the high-colored surface waters of Massachusetts. In one of these waters the albuminoid ammonia was 0.0296 in 100,000 parts, but the specimen remained unchanged, as to its dissolved nitrogenous matter, for months. By nearly all European standards this water, found to be harmless by public use, would have been condemned on account of its high percentage of albuminoid ammonia.

The highly colored waters of Southern swamps have an evil reputation, I am aware, and may deserve it on account of widely different organic contents. In the water just alluded to the largest amount of organic matter observed was 3.15 parts per 100,000, or 1.82 grains per gallon; if two quarts of this water were drunk in the day, less than one grain of vegetable matter would be taken into the stomach during the twenty-four hours.

Beyond the usual significance which "free ammonia" in water has, a new explanation has been found for the great increase observed in some deep ponds and reservoirs in the late autumn and early winter. In the course of an interesting and important examination of deep ponds and reservoirs at different depths, it was found that in ponds

of a depth greater than twenty feet the bottom water remains stagnant for about seven months in the warmer part of the year, while the upper layers are kept in circulation by streams entering the pond and by winds. In some ponds, especially in those where the bottoms contain much organic matter, the lowermost layers of water, to which the air does not have access, become very foul, contain much free ammonia, no dissolved oxygen, and smell of carburetted and sulphuretted hydrogen. The cause of this stagnation is the greater warmth of the upper layers during the summer; as the atmosphere grows colder, about the first of November, a current is established from the surface down to the level at which water of the same temperature is found. The pond is, in fact, turned over, and the lower foul layers come into circulation and cause a marked deterioration in the water near the surface.

The oxidation of ammonia into the various nitrites and nitrates signifies the complete reduction of the organic matter of which the nitrogen was a part. The sewage-polluted stream, which has reached the last stage of oxidation of its nitrogenous matters, shows "the previous sewage contamination" of Frankland, and remains a suspected, though not necessarily dangerous water.

Upon the question of the sanitary importance of the dissolved mineral matter in the waters of the State, there is nothing to be added to the recorded experience of other communities. In no one of our water-supplies is the amount of such matter as great as in many of the approved and apparently healthful supplies of the world. A careful examination through a long series of years of the towns which have a relatively hard water, and of those where the water used is soft, has revealed no differences in the kind or severity of the diseases prevalent in them, except the inevitable inequalities that may fairly be referred to other conditions known to affect human health.

Ground and surface waters differ so essentially from each other that the same standards cannot be used with both. While surface waters may safely contain organic substances in considerable quantity, may be high-colored, may exhibit animal and vegetable forms of life, a normal ground water should, on the other hand, have no color, no life, and little or no organic matter. Though both waters have the same origin, and interchange their places at times, they are still easily distinguishable from each other.

The changes that take place in them are effected in great part by the processes of filtration through soil, and upon the character of this depends the completeness of the process. The microörganisms, which are the active workers in the changes of the organic contents, find the most favorable conditions for efficiency in a soil of considerable porosity and of a sandy or gravelly character.

If the organic matter in a water has been completely oxidized by filtration through soil, under favorable conditions, all of its nitrogen will appear in the form of nitrates.

Experiments upon the purification of sewage by intermittent filtration at Lawrence have been conducted since 1887, and it may fairly be claimed that they constitute, even in their present form, an important addition to our knowledge of the processes by which nitrogenous matters are modified while percolating through porous ground, and give a more satisfactory explanation than we have yet had of the results of chemical analysis of ground waters.

When a carefully adjusted quantity of sewage is allowed to filter through five feet of suitable material, and these applications of sewage are separated by sufficient intervals of time, an effluent has been obtained which is as free from organic matter, from ammonia, and from nitrites as many natural spring waters are. It must constantly be borne in mind that though these great changes are effected by a comparatively thin layer of sand and in a brief space of time, still the contrivance is of the most delicate nature and can easily be deranged by a too great amount of fluid applied, or by insufficient intervals of time between the applications.

All that has been found true of the difficulty of adjusting the action of this artificial arrangement will be also observed in the case of the well which drains a soil contaminated by human waste.

Of great importance in this connection is the demonstration of the inability of garden soil to purify sewage, even when the sewage is applied in small quantities. This proof is of the greater consequence from the fact that such soils are commonly thought to possess great capacity as purifiers.

Experiments conducted with great accuracy show that filters composed of gravel-stones, of which none were less than three-fourths of an inch in diameter, may be so used as to be efficient purifiers of sewage. The intermittent filtration of sewage by soil, when properly

carried on, is not a straining through fine pores, and is to a slight degree only mechanical.

The straining of sewage through filter-paper in the laboratory removed from the sewage 11 per cent. of the sum of the ammonias, and about 80 per cent. of the bacteria; but the slow moving of thin films of sewage over and between the surfaces of gravel-stones of the size above indicated caused the removal, day after day for months, of 97 per cent. of the sum of the ammonias, and of 99 per cent. of the bacteria.

The process is not a mechanical holding back of these substances, but a change in which the organic matter is oxidized and appears as mineral matter in the purified effluent. The quantity of sewage that can be purified in a filter of this sort is large. It was found that the high standard of purification above stated could be maintained for months when sewage at the rate of 126,000 gallons per acre per day was applied for six days in the week. The effluent in this case was a pure, bright water comparing favorably, so far as chemical and bacteriological tests are to be depended on, with the waters which man willingly drinks. The process of purification by nitrification is not prevented by the cold of a New England winter, provided the surface of a properly constructed area can be protected from the snow.

The records of medical experience are full of instances of the harmful effects of polluted ground waters, far greater in number than those which we have reason to believe are due to surface waters. Investigation almost invariably reveals in the former cases the entrance, by a more or less direct channel, of drainage from a privy vault, cesspool, or defective sewer. Every well in an inhabited district is exposed to the danger of this kind of pollution; it is, therefore, a subject of the greatest moment to know the degree of confidence that can be placed in the information given by a chemical analysis. If the organic matter and the earlier products of its decomposition were the only harmful agents, then we should reject the waters which contain free or albuminoid ammonia or nitrites, and admit those only in which the nitrogen is represented by the nitrates. If, on the other hand, the danger of these waters resides in the bacteria present—these are not revealed by chemical analysis—then chemistry offers here, as in surface waters, only indirect evidence of their condition. It is not now possible for us to say that the life of the pathogenic bacteria ceases with the con-

version of the organic matter into nitrates, for there is no well-proved connection between the life processes of the saprophytic bacteria of sewage and the limited number of bacteria known to produce disease in man. It has been asserted, upon good authority, that the bacteria of decomposition create conditions unfavorable to the life of the bacteria of disease, and that the latter necessarily perish when the former have done their work.

It is well known, however, that an intermittent filter-bed does not do its work thoroughly until a certain amount of sewage has been passed through it, and until a sufficient period has elapsed for the establishment therein of the organisms that cause nitrification. It is, therefore, evident that not all organic life perishes with the saprophytic bacteria, and possibly the bacteria of some of the infectious diseases may be equally tenacious of life.

Many attempts have been made to discover and isolate the nitrifying organisms. Few researches in this field have been more laborious or more full of disappointments. It has been clearly shown that the ordinary bacteria possess little, if any, power in the processes of nitrification. Experiments in the laboratories of the State Board of Health confirm this opinion. Mr. E. O. Jordan and Mrs. E. H. Richards have lately conducted there an investigation which leads them to the following conclusion, reached independently of the nearly contemporaneous researches of the Franklands and Warrington in England, and Winogradsky in Zurich. They obtained, after many attempts, two solutions that nitrified well, but gave no growth in ordinary gelatin plate cultures. Microscopic examination of these solutions showed them to be inhabited by a particular form of bacillus, and by that alone. These bacilli are short, of a slightly oval shape, and vary from 1.1μ to 1.7μ in length; they are about 0.8μ to 0.9μ broad. They are grouped very characteristically in irregular clumps, and are held together by a jelly-like material. Each aggregation is a typical zoöglœa. These masses of zoöglœa, obtained as a pure culture from a nitrifying solution, bear a striking resemblance to the zoöglœa discharged from the experimental filter-tanks at Lawrence.

If normal ground waters cannot be obtained for a supply, the time and distance from the sources of pollution should be as great as possible. Waters with high nitrates should be looked upon with suspicion, for though well purified to-day the source of pollution is not

far off, and an accident may, at any moment, make a connection too direct to permit efficient oxidation. This reduction of organic matter can only be assumed to take place in porous soil with thorough exposure to the air. The condition of things is very different when drainage enters the soil at a considerable depth below the surface, removed from free contact with the air, and makes its way through a limited channel in a continuous stream. None of the conditions of good filtration are present here, and the effluent is always a source of danger.

From this hurried statement of some of the results of observations in Massachusetts it has been apparent, I hope, that while limitations to the use of chemical analysis have been indicated, there has been no intention to diminish its real importance. A single chemical determination of the constituents of a given specimen of water may point out the way to obtaining more complete information about the supply; it rarely enables us to render judgment. All that the most complete analysis can tell us, is that the water was good or bad at the time when the specimen was taken. In our regular series of analyses single examinations have often shown waters to be in good condition when an inspection of the whole series would reveal the presence of the products of decomposition in considerable amount. With our present knowledge of the waters of the State it has become possible for us, on the strength of the evidence afforded by chemical analysis, to decide definitely upon the question of the pollution of water by sewage.

The interest of these inquiries of the Board of Health of Massachusetts rests somewhat on the fact that this State is, with the exception of Rhode Island, the most densely populated State of the Union, and the evils of river pollution should, naturally, be at their worst there. There has, however, been much legislation for the protection of public water-supplies throughout the State, and instances of the direct addition of sewage to streams used as sources of supply are rare.

The Connecticut and the Merrimac, the largest rivers of Massachusetts, have their origin far beyond the State limits; they are not protected in the States through which they have already flowed before reaching our borders; and have not been, in consequence of this fact, included in our protective legislation. No Massachusetts municipality takes water for its domestic use from the Connecticut. On the Mer-

rimac, however, two large manufacturing cities, Lowell and Lawrence, do draw their domestic supplies from the river.

Three large water-powers on the Merrimac, at Manchester, in New Hampshire, and Lowell and Lawrence, in Massachusetts, are thoroughly developed and utilized; the manufacturing wastes of all the mills upon the river, as well as all the sewage, wherever systems of sewerage exist, enter the stream. By the State census of 1885 there was on the river above Lowell a population of 230,000, or 58 persons per square mile; and above Lawrence a population of 363,000, or 80 persons per square mile. The average flow of the river at Lawrence per twenty-four hours has been at the rate of 9145 cubic feet per second, which is about four times the low-water flow in an ordinary dry season. The population of Lowell by United States census of 1890 is 77,696, and that of Lawrence 44,654. The Merrimac has always been regarded as a marked instance of the capacity of a large body of water moving rapidly to purify itself. There is nothing in the appearance or taste of the water to deter a community from its use, nor does the chemical analysis indicate a water too polluted for drinking; it compares favorably with the poorer half of the surface waters of the State.

Many public water-supplies of large cities throughout the United States are taken from streams which present conditions of pollution similar in kind, and possibly greater in degree.

It will, therefore, not be inappropriate to state some of the results of an examination of the statistics of disease in these two cities, and attempt to show the connection of one infectious disease, at least, with the domestic use of the river-water.

The average death-rates of Lowell and Lawrence for the census years 1870–75 and 1880–85 were, for the former city, 21.6 per 1000, and for the latter 22.1 per 1000; the average for the whole State for the same years being 20.1 per 1000.

One disease was conspicuously prominent in the returns from these cities—typhoid fever; the diarrhœal diseases were also excessive, but the excess was not so marked in a succession of years as it was in the case of typhoid fever; moreover, the diseases brought together in this group cannot readily be separated from it and brought into comparison with the same diseases in other communities.

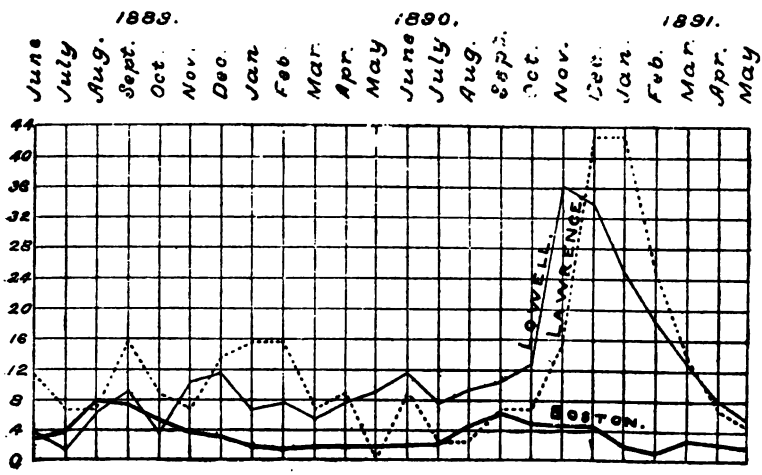
The average death-rate from typhoid fever, of all the cities of Massachusetts, for twelve years, from 1878–89, was 4.62 per 10,000; for the same period the rate in Lowell was 7.63, and in Lawrence 8.33 per 10,000. The deaths from this disease in the year 1890 have not been included in these comparisons, because Lowell and Lawrence experienced in the past year an epidemic of typhoid fever of great severity, while throughout the State at large the disease was not unusually prevalent.

The introduction of public water-supplies throughout the State has had the same marked influence that has been observed elsewhere upon the prevalence of typhoid fever. An examination of the death-rates of more recent years will show that these two cities, instead of a progress toward immunity from the disease, are steadily losing ground. If we look at the death-rates of the four years 1886–89, we find the average rate from typhoid fever to be 9.55 per 10,000 for Lowell and 10.30 for Lawrence, while all the cities of the State for the same period have a rate of 4.59 per 10,000.

The amount of sewage that has entered the river during the past three years is estimated to average one gallon in every six hundred gallons of water in the stream at Lawrence; and, as above stated, this impurity is no greater than that existing in half of the supplies of the State derived from ponds and streams.

Typhoid fever begins to be prominent among the diseases of the State toward the end of August; the highest death-rates from it are reached in September and October. The decline begins in November, and the lowest point is reached in January and February. The death-rates of Lowell and Lawrence from this disease do not vary essentially from those of the State as a whole up to the month of September. From this month on, a condition of things exists in the two cities distinct from what is observed elsewhere in the State; that is to say, the deaths from typhoid fever continue to increase in number in Lowell until December, and in Lawrence till a still later date. This difference in the months of greatest prevalence is made very conspicuous in the accompanying diagram, which has been prepared for a forthcoming report of the State Board of Health by H. F. Mills, C.E., a member of the Board. Herein is shown the number of deaths from the disease per 100,000 inhabitants for each month, in Boston, Lowell, and Lawrence, from June, 1889, to June, 1891.

The death-rate in Boston from the disease is nearly the average rate of the whole State. It will be seen that in 1889 and 1890 there came at Lowell higher death-rates in November and December, and in Lawrenec a steadily increasing rate through November and December, which did not reach its maximum till December and January, or even later. That is to say, we find such a condition of things to exist as we should expect to find if a disease capable of being transmitted by the infected excreta of those sick with it had prevailed during the late summer and early autumn at some point on the river above Lowell. The infected discharges of the sick in Lowell would, with the sewage of the city,



Number of deaths from typhoid fever in 100,000 inhabitants for each month in Boston, Lowell, and Lawrence.

enter the river and, nine miles lower down, would be taken into the water-supply of Lawrence, causing there a later outbreak of the same disease that had prevailed in Lowell. The river-water is not used for domestic purposes below the city of Lawrence, and it is suggestive that the city of Haverhill, with a population of 27,000, not substantially differing from the people of Lowell and Lawrence, situated also on the Merrimac, nine miles below Lawrence, should have had a general death-rate in the last census year of 17.8 per 1000, and a typhoid fever death-rate of 3.33 per 10,000 in the year 1889.

The public water-supply of this last city is taken, not from the Merrimac, but from sources remote from the river.

An attempt was made, and with apparent success, to prove the existence of cases of typhoid fever at points on the river above Lowell, and to show that the discharges from the bowels of the sick had found immediate entrance to the river.

The New Hampshire cities which empty their sewage into the Merrimac did not appear to have had, in the year 1890, an unusual amount of typhoid fever. There had been, however, in the months of August and September, several well-defined cases of the disease among operatives in some manufacturing establishments situated along the course of Stony Brook, a small affluent of the Merrimac, entering the river at a point about two and a half miles above the in-take of the Lowell water-works. It was proved that some of these persons had, in the early stages of the disease and while they were still able to work, made use of privies which overhang the brook.

The temporal connection of these cases was such that, with the allowance of two weeks for the time occupied by the incubation and early stages of the disease up to the time of taking to the bed, we find an apparently direct relation to the serious increase of the disease in Lowell in the latter part of October, 1890.

The amount of infective matter did not at this time appear to be sufficient to pollute the river, to the same serious extent, at the in-take of the Lawrence water-works, nine miles below Lowell. With the increase of the disease in Lowell there came the growing specific pollution of the river, and the people of Lawrence began, in turn, to suffer.

It will be noted that the material of infection survived the passage between the two cities at a season when the temperature of the water must have been at a point not considered favorable to the growth of the bacillus of Eberth. The temperature of the river in November, 1890, ranged from 45° to 35° F., and the time which the water would take for its flow from the sewer outlet at Lowell to the in-take at Lawrence would be eight hours. The stay of any portion of the water pumped to the reservoir and entering the service-pipes would be limited, for the larger portion of the city, to a week; the more remote portions of the city would not be reached by the same water under a fortnight. Experiments have been made which show that in Merrimac river water kept steadily at the temperature of November, 1890, the bacillus of Eberth survived until the twenty-fourth day, though steadily decreasing in number.

The numbers counted were as follows:

First day	6120 per cubic centimetre.
Fifth day	3100 " "
Tenth day	490 " "
Fifteenth day	100 " "
Twentieth day	17 " "
Twenty-fifth day	0 " "

It early became evident that during these epidemics, given a number of cases which apparently had their origin in an infected water-supply, you would find very many more subsequently occurring, which were undoubtedly transmitted from the sick to their attendants, and to those who stood in more or less intimate relations to the sick. An examination of the milk routes showed that they had not been the channels of communication.

The search for the typhoid bacillus began, as is usually and perhaps necessarily the case, after the epidemic was thoroughly established; in but one of the many specimens of water taken from the river at Lawrence was the bacillus of Eberth discovered and identified by the required tests. It may here be said that instances of the discovery of this bacillus in water-supplies during the Massachusetts epidemics are rare.

Let us compare with this river-water, which appears to have been the principal agent in bearing an infectious disease from one city to another, the water from a well in the city of Lowell used by a large number of persons.

This well attracted the attention of the Board of Health, while engaged in a general examination of public wells, by reason of the following chemical analysis:

Loss on ignition.	Fixed.	Free ammonia.	Albuminoid ammonia.	Chlorine.	Nitrates.	Nitrites.	Oxygen consumed.
3.8	86.8	3.224	0.0880	11.60	5.80	0.0022	0.23

The analysis of the water supplied to the city of Lawrence during the month of November, 1890, is added by way of comparison:

Loss on ignition.	Fixed.	Free ammonia.	Albuminoid ammonia.	Chlorine.	Nitrates.	Nitrites.
1.10	2.65	0.0014	0.0136	0.18	0.0090	0.0002

In the investigation it appeared that this well, by reason of its cooler water, was much resorted to in summer by all the people in the vicinity. The character of the water was known to the local sanitary authorities, the discontinuance of its use had been ordered, and a chain and lock had been placed upon the pump. So much feeling was excited among the neighbors by the loss of a much prized and agreeable beverage that the pump was secretly unchained, and again became accessible to the public.

The well is in the centre of a thickly settled district; foul privy vaults are within fifty feet of it; a stable and hen-house are even closer; tenements crowded with occupants are within ten feet of it; and the soil in the vicinity is thoroughly polluted. It was estimated that about five hundred persons in the immediate neighborhood might be fairly assumed to be more or less common users of this water.

For the purpose of getting a better appreciation of the deleterious effects of this water, another collection of persons was taken of the same social relations, dwelling under similar local conditions, and differing from the first mentioned district only in the circumstance that the water therein used came exclusively from the public supply. The districts selected—A and B—contained, respectively, 462 and 478 individuals, divided as follows:

"A"		"B"	
Men	117	Men	136
Women	183	Women	202
Children under 14 years	162	Children under 14 years	140
	462		478

The diseases ordinarily prevalent in the two districts are not essentially different; their death-rates for a period of five years are, in the average, for "A," 29.09 per 1000, and for "B" 28.99 per 1000; that is to say, this well has been without appreciable effect for the last five years at least. A death-rate of 29 per 1000 is probably as low a rate as such a tenement-house population obtains in any of our larger cities.

So far as this well was concerned there is not sufficient evidence to show that it had any influence upon the death-rate from typhoid fever. Not a single case of the disease had occurred in district "A" in 1890 up to the first day of November, when the highest point of the epi-

demic in Lowell was reached. Typhoid fever has occurred in both districts. In the three years from January 1, 1888, there were 17 cases, with 3 deaths, in "A," and 15 cases, with 4 deaths, in "B"; a proportionately larger number of cases and deaths, for this limited population, than obtained for the whole city. The numbers dealt with are too small, however, to allow any conclusions to be drawn from proportions gained by averages in these few years. The figures are used only to show that there is no apparent difference in the sanitary condition of the two groups, and also to add an emphasis to the original statement, that the most polluted water yet discovered in the State is not only not offensive to the senses, but has had little, if anything, to do with causing disease or death.

What the result would be if this experiment were suffered to go on, cannot, I think, be a matter of doubt. The experience of every community in our State has proved to the satisfaction of competent observers that, sooner or later, the unknown something will become a part of the water, will not be removed by the imperfectly filtering soil, and an epidemic will be the result.

The example shows, again, that human senses may not detect the most serious pollutions, and that a contaminated water will not produce disease until it it is specifically infected.

The influence that a general water-supply can have upon the health of the community using it was well shown by an experience of the town of Adams, where on June 15, 1880, an epidemic suddenly broke forth which lasted a few days and then disappeared as suddenly as it came.

The disease came on without warning, the attacks were of short duration, and none were fatal. They consisted, for the most part, of vomiting, diarrhœa, and pain in the stomach and bowels. Beginning on the fifteenth of June, on the nineteenth the epidemic was practically over.

Adams is a manufacturing town in the northwestern part of the State. The water-supply came from a small reservoir among the hills above the town, and was derived from an unpolluted gathering ground. The water had always been found, on laboratory examination, to be of great purity. A house-to-house examination of the town was made as soon as the facts were brought to the attention of the Board of Health. The whole number of the sick was found to be

1112, or 24 per cent. of the people actually seen by the inspector. The apparently well-justified conclusion was, that every recognized agent injurious to health could be excluded, with the exception of the public water-supply. It should be added that the examinations were not entered upon until the epidemic was past, and it might well be that evidence of the existence of microscopic organisms had already vanished.

Upon two occasions the public supply of the city of Boston had become so offensive to taste and smell that its use was seriously limited. Anxious investigations were made, in both instances after the mischief had happened. Near the close of one of these periods of disaster, Prof. Remsen detected among the perishing organisms in one of the reservoirs the "spongilla," which was a sufficient explanation of the mischief. Such catastrophes are unendurable, and probably unnecessary.

Our experience has shown that the water from unpolluted deep ponds or deep storage reservoirs, where the soil and vegetable matter have been thoroughly removed, is satisfactory.

The troublesome growths of vegetable and animal forms of life, which occasionally take place in reservoirs and ponds, seem to stand in very close relation to the number of people living upon the drainage area. The nitrogenous waste matters, that always abound in the vicinity of human life, find their way, more or less, directly into the water and furnish the food required for the growth of organisms. This troublesome growth is especially liable to happen where the population on the water-shed exceeds three hundred per square mile.

It has also been most conclusively shown, that waters which have become well purified in filter galleries, or by passing through filter beds, and are entirely acceptable to the senses, become, when exposed to light, in an open reservoir, subject to a bad taste and odor produced by the algæ and other organisms, for which such waters are good nutritive media. In fact, under such conditions of storage, the number of organisms is sometimes greater than is found in any other source of supply. The remedy of covering the reservoir, so as to exclude light, has been adopted with success.

The imperfectly filtered waters, in addition to the always present danger from the organisms associated with disease, are likely to become extremely offensive from the growth therein of crenothrix, which

has the peculiar property of taking into its structure the iron which may be dissolved in the water and of depositing it in the form of an oxide, so that the water also becomes useless for the laundry. Crenothrix flourishes upon extremely minute quantities of dissolved organic matter, and every source of such material must be carefully excluded. Objectionable as the presence of the organism is, we have, thus far, failed to find evidence of its harmfulness.

Among the experimental researches at the Lawrence station, there are several of which the results thus far obtained may be of interest to the profession.

It seems to have been shown that heat applied to solids or fluids containing organic matter, for the purpose of sterilization, has also the effect of rendering this organic matter a better food for bacteria, when these secure admission to it.

Attempts have been made in the last few years, both here and abroad, to determine the safety or danger of a given water by injecting a minute portion of it into the abdominal cavity of a rat, the water having been previously mixed with sterilized bouillon and kept in a thermostat at the temperature of the human body for twenty-four hours. Our experiments with this method have not been favorable to it. Waters polluted with discharges from the bowels of typhoid-fever patients have proved fatal, in all cases, to the animals; but so too have waters known to be safe, when contaminated by addition of a pure culture of "bacillus coli communis." It is true that the assertion has been lately made that this microörganism may, under certain conditions, become pathogenic. However this may be, bacillus coli communis is generally found in our sewage-polluted streams.

A form of water which has assumed very important relations to human life, is ice. Even the people who occasionally interest themselves in doubting the purity of the water they drink, rarely inquire as to the origin of the ice used. As a matter of fact, this often is taken from water so polluted that the suggestion of using the water itself for drinking would not be entertained for a moment. The process of freezing does remove a considerable portion of the impurities in the water, but this purifying effect is found to be greater upon substances in solution than upon those in suspension. In an average of the contents of the waters and the ice formed thereon, it was found that the snow ice contained 69 per cent. of the organic im-

purities of the waters, as shown by the sum of the ammonias; while ice free from snow and bubbles has but 6 per cent. of these impurities.

Eighty-one per cent. of the bacteria of the water remained in the snow ice, and but 2 per cent. in the clear ice.

We have no evidence, though, that this much-reduced number of bacteria may not include the pathogenic forms, some of which are known to be capable of withstanding, for long periods, a freezing temperature.

THE PATHOLOGY OF PERNICIOUS ANÆMIA.

By J. P. CROZER GRIFFITH, M.D.,
CLINICAL PROFESSOR OF DISEASES OF CHILDREN IN THE UNIVERSITY OF PENNSYLVANIA,

AND

CHARLES W. BURR, M.D.,
OF PHILADELPHIA.

ALTHOUGH the causes and nature of the various affections which may be called forms of anæmia are at present so obscure, yet, for purposes of study, some method of classification of these forms becomes almost a necessity. The difficulty of the subject is perhaps the reason for the number of classifications that have been proposed.

In a previous publication by one of us (*Cyclopædia of Diseases of Children*) anæmia was defined as a diminution of the blood *in toto*, or of its albuminous material, blood-cells or hæmoglobin, and a system of classification was suggested. We would now propose the following tabular scheme, which is somewhat modified from that in the publication referred to, and which we admit to be imperfect and only provisional:

- ANÆMIA
  - Non-cytogenic
    - Hæmolytic
      - Pernicious anæmia.
      - Other toxic anæmias.
      - Parasitic anæmias [some forms].
    - Oligocythæmic
      - Parasitic anæmias [some forms].
      - Post-hemorrhagic anæmia.
      - Anæmia from loss of albumin.
      - Anæmia from malnutrition.
  - Cytogenic
    - Oligochromæmic — Chlorosis.
    - Leucocytic — Leukæmia
      - Splenic.
      - Lymphatic.
      - Medullary.
    - Non-leucocytic
      - Simple constitutional anæmia.
      - Splenic anæmia.
      - Lymphatic anæmia.

The terms "primary" and "secondary" are best avoided altogether, as they have so frequently been misapplied. "Cytogenic" and "non-

cytogenic," though not interchangeable with them, are certainly preferable.

In the light of all that has been written, one might be disposed to regard the foregoing tabular classification as arbitrary and unnatural; and the opinion might be, as it has been, advanced that there are few sharp lines of demarcation between the various forms of anæmia. Thus, it has been maintained that chlorosis and pernicious anæmia are closely allied, and several instances have been reported in which a transition from one disease to the other had taken place. Luzet has published a most striking instance of this apparent transformation. Leukæmia was claimed by Wood twenty years ago to be nearly related to, or perhaps identical with, lymphatic anæmia, and there have been a few cases reported, as, for example, by Mosler and Fleischer, and Penzoldt, in which the latter disease seemed to be transformed into the former. Pernicious anæmia has in some instances appeared to be closely allied to leukæmia. Musser, for example, published a case in which the blood at one time indicated the existence of leukæmia, though the condition later appeared to be one of pernicious anæmia; and Leube and Fleischer have reported cases apparently the converse of this.

In spite of these seeming objections to the existence of different varieties of anæmia as distinct and independent diseases, we lean to the opinion that at least many forms are entirely separate entities. We certainly take the ground held by the majority of physicians that chlorosis and pernicious anæmia are widely separated from each other, and that the latter has certain peculiarities that sharply distinguish it from most other varieties.

Turning now more directly to the subject of this contribution—the pathology of pernicious anæmia—only the briefest review can be given of some of the different theories that have been held. Various propositions have been advanced, which have met with no general acceptance. Among these are the claims of Klebs, Frankenhäuser, Eichhorst, and Petrone that a species of cercomonas, or that micrococci, exist in the blood. The belief of Kjellberg, that the disease is an infectious one, belongs to the same category. By far the majority of writers, however, have for years regarded pernicious anæmia as a cytogenic disorder, a disturbance of the production of red blood-cells. Wood, in 1871, described the red condition of the marrow of the long bones, and

Pepper thought that this might be the starting-point of the disease; while Cohnheim, a year later, was inclined to view this condition as the specific cause. According to this theory the disease is a medullary anæmia, or, as some have called it, a medullary form of Hodgkin's disease. The probability of the truth of this seemed great, since in cases of pernicious anæmia no important post-mortem anatomical changes could be found, except the hyperplastic alteration of the bone-marrow. Later, however, doubt began to arise as to whether the medullary changes had any etiological connection with the disease. Cases of pernicious anæmia were described in which no such alteration existed, and Neumann, Litten and Orth, and others, found that this hyperplastic change takes place in other affections as well. Thus in animals such a red marrow may be produced by repeated bleedings. (Bizzozero, Salvioli, Litten, Orth.) Eichhorst and others entertain the belief that in pernicious anæmia the condition of the bone-marrow is purely secondary, the hyperplasia being only the evidence of the effort on the part of the hæmogenetic bone-marrow to supply by excessive production the great lack of corpuscles in the circulation. Mott echoes the same sentiment.

Still another view has been maintained by several writers (Russell, Henry, Mackenzie, Purser), somewhat of a modification of that of the cytogenic nature of the disease. It is that the affection is an altered and imperfect, rather than insufficient, cytogenesis, by virtue of which the red blood-cells are so badly made that they break down very easily. Russell is perhaps the strongest supporter of this view, and reports a number of observations opposed to the theory (presently to be discussed) of the purely hæmolytic nature of the disorder.

In this connection it may be stated that the alteration in shape of the corpuscles seen in pernicious anæmia is not at all characteristic of the disease. We have seen this alteration well marked in cases of extreme anæmia of other nature. The increase in the size of the corpuscles, and the occurrence of nucleated red blood-cells in the marrow and blood, are also very probably of a secondary nature, since they are not confined to this disease alone.

It would seem, then, that there is no change of the blood itself, or of the cytogenic tissues, which justifies the assumption that pernicious anæmia is a cytogenic disorder. At any rate, it is not proved that there is any disturbance of blood-formation, and, by the laws of logic,

the burden of proof rests upon those who assume that such a disturbance exists.

Omitting for the time the discussion of the published views that would ascribe at least some cases to the presence of bothriocephalus latus, or to atrophy of the gastric mucous membrane, we must, then, take up the consideration of the affection as one of a hæmolytic nature. This theory has been brought into prominence by the able researches of Hunter, though his investigations were not the first upon the subject. Quincke, in 1876, found a great increase in the amount of iron in the liver in three cases of pernicious anæmia, and in 1877 Rosenstein confirmed this observation. Later, as a result of their studies, Quincke and Peters concluded that this increase is a constant and characteristic feature. Peters found that the increase might occur to a varying degree in other disorders. He attributed it, as did Quincke, to an excessive destruction of red blood-cells. Stahel, too, in a case of pernicious anæmia, found a very great increase in the amount of iron in the liver, but none in the spleen.

These investigations seemed to be almost forgotten and their bearing not appreciated, until Hunter published his observations, which are too fresh in the minds of all to allow of more than the briefest reference. Hunter examined the viscera in a number of cases of pernicious anæmia, and found a remarkable deposition of iron-pigment in the livers of all of them. The iron existed in a granular form within certain of the hepatic cells, viz., those of the outer and middle zones. In certain other diseases, as in cirrhosis of the liver, malaria, and chronic venous congestion, he found at times an increased amount of iron, but never to such a degree, and never exhibiting the peculiar arrangement which he regards as characteristic of pernicious anæmia. He regarded the granular matter as a decomposed hæmoglobin, since hæmoglobin itself will not answer to the reactions for iron which he employed, and which will presently be described. In some cases he was able to discover the same pigment in the cells of the renal convoluted tubules. He found no increase of iron in the spleen in any of his cases. He explains this on the ground that, though the hæmoglobin is set free in the spleen or between it and the liver, it remains hæmoglobin until it reaches the latter, and consequently gives no characteristic reaction for iron. The urine of his patients was of a dark color, due to the presence of a large amount of pathological urobilin,

which is probably a still further alteration of hæmoglobin, through the medium, however, of the bile-pigments. In one carefully observed case the urine contained an increased amount of iron, together with two ptomaines never produced except by the action of certain micro-organisms. He concludes, therefore, that pernicious anæmia is the result of an excessive destruction of blood in the portal circulation, and that this destruction is due to the absorption from the alimentary tract of certain ptomaines—produced, perhaps, by the action of micro-organisms.

By a series of experiments upon animals he endeavored to produce artificially in them the symptoms and pathological appearances of the disease. For this purpose he introduced into the circulation various hæmolytic substances; but found that though some of them were capable of producing hæmoglobinuria, one, toluylendiamine, by its special action upon the blood and the liver, was efficient in producing a condition of this organ identical with that seen in cases of pernicious anæmia.

Other observers have since maintained the hæmolytic nature of pernicious anæmia, corroborating the statements made regarding the condition of the liver found post-mortem in this disease. It is true that, among these, Russell, while admitting the excessive hæmolysis which takes place in the disease, believes, as we have said, that this depends upon a defective hæmogenesis, and claims, from his study of the liver and spleen in forty-four cases of other disorders, that the excessive iron-reaction is not found in pernicious anæmia alone. He has found an increase in the amount of iron in the spleen also in one case of pernicious anæmia, as well as in a number of cases of other disorders. Mott seems to incline to the view that the disease depends upon the formation of some poison or ferment connected with micro-organisms. In one case he found no iron in the spleen, though in another a deposition of pigment was observed.

Our own observations have little or nothing new to offer, and are of value only in so far as they may confirm or oppose the meagre data as yet obtainable toward a more perfect understanding of this still very obscure subject. They have been confined, for the most part, to the question of the presence or absence of iron in the liver in pernicious anæmia and in other diseases, particularly forms of anæmia. We have also in progress a series of experiments upon animals, but,

as they are not yet completed, the results will be reserved for future publication.

The reagents which we have employed have been those recommended by Hunter, Peters, and others. Sections of liver from specimens hardened in alcohol were, after washing in water, immersed for from five to fifteen minutes in a rather strong aqueous solution of potassium ferrocyanide; then, without washing, these were placed for an equal time in a weak aqueous solution of hydrochloric acid. The altered blood-pigment characteristic of pernicious anæmia contains iron in a form which, treated in this way, develops the well-known Prussian-blue reaction, and becomes visible as granular matter of a blue color within the hepatic cells. The sections can now be passed through the necessary steps preparatory to preservation in balsam. The iron may also be rendered visible by immersing the sections in a freshly prepared solution of ammonium sulphide, by which means the sulphide of iron will be produced, and will appear as a heavy, black precipitate within the cells. We have, for the most part, used the treatment with potassium ferrocyanide.

The livers from three cases of pernicious anæmia have been studied: the first from a patient of Dr. Morris J. Lewis, the second from a case occurring in the Hospital of the University of Pennsylvania, and the third from a patient of Dr. J. H. Musser. It is sufficient here to say that examinations of the blood were made in all of them, and that, in this as in other respects, the symptoms were those characteristic of the disease. We shall confine ourselves to the condition of the liver with regard to the presence of iron.

CASE I.—The hepatic cells of the outer and middle zones of the lobules were very full of iron-pigment, the amount constantly diminishing in the inner zone as the central vein was approached, so that in the greater number of the cells of this zone there was no appreciable amount of iron present. The iron was in the form of minute, irregularly shaped granules. These, closely aggregated, seemed to form a continuous band running along the centre of the irregular bands of hepatic cells. No pigment could be found in the capillary bloodvessels or bile-ducts. Besides the iron-pigment, a granular blood-pigment of a yellow color, such as is frequently visible in sections of liver, was discernible in parts of the sections, chiefly in the region nearest the central vein. The wall of the central vein was stained a blue-green color in the specimens treated with ferrocyanide, but no granular matter could be detected in it.

CASE II.—The appearance of the liver was almost identical with that of the preceding case. In this case, too, there was noticeable the presence of a considerable amount of yellow pigment, chiefly in the inner zone of the lobule, which was not affected by the potassium ferrocyanide.

CASE III.—The condition of the blue-stained pigment in this case was almost identical with that in the preceding cases, though perhaps the amount was not so great.

The spleen was examined in the first case, and found to contain no increase in the amount of iron. The kidney in the first case exhibited a slight deposit of iron-pigment in the cells of the convoluted tubules. In the second case no such deposit could be found.

As check observations upon these, we have examined livers from a large number of cases of different diseases, making an especial effort to obtain preparations from patients affected by some disease attended with anæmia. It would unnecessarily occupy time to detail the results of these investigations. It is sufficient in general to say that in not a single instance was the characteristic pigment found in amount at all comparable with that seen in pernicious anæmia, nor did it present the characteristic arrangement. In most cases it was either entirely absent, or present in very small quantity. It is naturally to be expected that at least a small amount of pigment would normally be found in the liver, if, as supposed, this organ is the normal seat of blood destruction.

A few of the cases deserve a somewhat fuller reference.

1. In a case of cancer of the liver in which the connective tissue greatly preponderated, large masses of yellowish pigment were observed in carmine preparations. These were scattered irregularly throughout the sections, either among the liver-cells or in the connective tissue of the growth. They were apparently the result of hemorrhages. Sections treated with potassium ferrocyanide exhibited these masses stained blue.

2. On the other hand, a case of emphysema, with dilated heart, exhibited, as might be expected, considerable yellowish pigment, situated chiefly in the cells about the central vein. When treated with potassium ferrocyanide no iron reaction whatever was discoverable.

3. Another very interesting specimen was from a case of pernicious malaria, which had been under the care of Dr. George Dock, then of Galveston, Texas. The patient had presented evidences of excessive hæmolysis occurring in the general circulation, as shown by the

presence of hæmaturia, and probably of hæmoglobinuria as well. The number of red blood-corpuscles was greatly diminished, and toward the end of life leucocytosis developed. The sections of liver in this case exhibited a large amount of deep-black granular pigment, the histological arrangement of which we shall not enter upon, further than to say that no such distribution was present as in cases of pernicious anæmia. Sections of liver treated with potassium ferrocyanide exhibited a considerable amount of iron-pigment in the hepatic cells. The black pigment was entirely unaffected by the reagent.

Other cases might be cited in further illustration of the point we wish to emphasize, viz., that various sorts of pigment may occur in the liver, only some of which give the ferric reaction. The black pigment of this third case gave no such reaction. In each of the first two cases a yellowish pigment was visible in carmine preparations. When treated with the ferrocyanide this became blue in the first case, but was unaffected in the second. As a rule, the yellow pigment, seen so often in livers, does not react to the ferric test. In two of the cases of pernicious anæmia reported, this pigment was present in the inner zone, and the blue iron-pigment in the outer and middle zones.

This variation in the nature of the pigments is in accord with the results of the researches of Neumann, who has shown that there are two forms of pigment in the body; the one, which he denominates "hæmosiderin," giving an iron reaction, and the other without such reaction.

4. In connection with the last case, in which hæmolysis occurred in the systemic circulation, sections from the liver of a case of Dr. B. C. Hirst's were of extreme interest.

This was an instance of infectious hæmoglobinæmia of the newly born (often, though we think unfairly, called Winckel's disease). In this instance the liver exhibited no iron at all. The kidney exhibited a decided blue-green tinting of the convoluted tubules, and, in some parts, of the loops of Henle, though the Malpighian tufts and the collecting tubules were almost entirely free from it. Nowhere, however, was there any evidence of any actual deposition of granular pigment, even when high amplification was employed.

We have already stated that a deposition of granules was present in the kidney of the first case of pernicious anæmia reported.

It would therefore appear from the third and fourth cases, the first of which was probably an instance of hæmoglobinæmia, and the second certainly so, that hæmoglobin set free in the systemic circulation is not deposited in an altered form in the liver nor reaches the kidney in such a condition that it is found there in a characteristic granular form. On the other hand, in pernicious anæmia hæmoglobin set free in the portal circulation does become altered in a peculiar way in or before reaching the liver, so that it is either deposited there, or, if in too great excess to be disposed of entirely there, passes into the systemic circulation in such a changed form that it is not excreted by the kidney as hæmoglobin, but as some other substance (pathological urobilin), while some of it is deposited in the renal cells in a chemical form similar to the granular matter in the liver. The reason for this difference between systemic and portal hæmoglobinæmia does not seem clear, nor can we explain why the spleen occasionally contains pigment in pernicious anæmia and at other times not.

Besides conditions in which hæmoglobinæmia occurs, those disorders commonly ranked as "diseases of the blood" were of especial interest to us, particularly in view of the claims that have been advanced that they were closely allied to pernicious anæmia, if not, indeed, capable of being transformed into it.

5. Sections of the liver from a typical case of lymphatic anæmia were treated with potassium ferrocyanide. The lymphatic tissue present was entirely free from iron, as were also the hepatic cells, except those upon the extreme periphery of the lobules. Here a circle scarcely wider than the diameter of one or two cells exhibited a decided deposit of iron-pigment, though not at all comparable in amount to that seen in pernicious anæmia.

6. Sections of the liver from a case of leukæmia were entirely free from iron.

It appears therefore that there is no likeness between pernicious anæmia and at least two of the cytogenic anæmias.

7. Another interesting case exhibiting a marked increase of the amount of iron in the liver was a very unusual one of complicated ulcerative endocarditis, in which during the life of the patient there had been reason to believe that abnormal destruction of blood had been in process in the general circulation. Nevertheless the pigment was deposited in irregular foci entirely without reference to the struc-

ture of the lobules. The amount of iron by no means equalled that in the specimens from pernicious anæmia.

Livers were examined from several cases of Bright's disease and of phthisis and no iron found. The liver also from a case of cancer of several of the abdominal viscera, in which the anæmia and cachexia had been exceedingly well marked during life, failed to exhibit any iron. A case of anthrax and one of gumma of the liver were without iron.

Besides livers from persons not anæmic, we have then examined the organ in a number of varieties of anæmia, viz., hæmolytic anæmia (pernicious anæmia, pernicious malaria, infectious hæmoglobinæmia); anæmia from loss of albumin (Bright's disease); anæmia of malnutrition (cancer, phthisis); leukæmia; lymphatic anæmia. In no instance was iron found in the liver to the extent or with the characteristic distribution seen by us and reported by others in cases of pernicious anæmia.

CONCLUSIONS.—Is it justifiable to consider pernicious anæmia a distinct disease, and if so, what is its nature? Our experience seems to corroborate the view that there is in this disorder a deposition of iron in the liver unlike that observed in any other, and that—as a deduction from this and certain other conditions found—pernicious anæmia is a form of hæmolysis. It is therefore a non-cytogenic anæmia. Whether there exists any defect in the formation of the corpuscles that predisposes to their destruction, when the proper destructive agents are brought to bear, it is as yet impossible to determine. There seems to us no good reason for this assumption.

In one light it might be claimed that the disease, broadly considered, need not be a unity—that is to say, there is no reason why but a single poison should produce the characteristic destruction of blood. For example, a condition closely resembling pernicious anæmia in the pathological changes may be produced in animals, as Hunter has shown, by the administration of certain hæmolytic agents, such as toluylendiamine. This artificial disease is in one sense, in fact, a pernicious anæmia. Pyrodin, also, has produced extreme anæmia in man, as was shown by the case of Renvers, in which the number of red blood-cells per cubic millimetre fell in three days from 4,000,000 to 2,800,000.

The cases of pernicious anæmia reported as cured by the expulsion of tapeworms probably owed their symptoms to the absorption from

the intestine of some poisonous product produced by the worm. Had the patients died, it is at least possible that an increase of iron in the liver would have been found, particularly as the poison absorbed would have been acting within the portal circulation. These, too, might in a wide sense be called instances of pernicious anæmia. Again, the cases of what seemed to be pernicious anæmia due to atrophy of the gastric mucous membrane were probably the result of the absorption of some product of the decomposition of food in the stomach, since dilatation of the stomach, with the consequent putrefactive changes, is a characteristic symptom of atrophy of the gastric mucous lining. The anæmia is certainly not one of inanition. A very analogous condition is that reported by H. Meyer, in which the most characteristic symptoms of pernicious anæmia were promptly relieved by a single washing of the stomach, doubtless thereby removing some poisonous product of decomposition which was being absorbed and was destroying the blood corpuscles.

As we have said, all these varying conditions might be considered instances of pernicious anæmia taken in a broad sense of the term. Are we then to consider the disease as not having an individual existence on the ground that it may have these various causes? Should it possibly be looked upon as a symptomatic condition of these different affections? We think not. The fact of the existence of tapeworm, or of gastrectasia with consequent fermentation, or of other conditions *without* the symptoms of pernicious anæmia, indicates that its peculiar complex of symptoms is not a necessary sequence to their existence. Pernicious anæmia is rather to be looked upon as a distinct disease which may arise whenever some certain poison is present and is absorbed. When its symptoms are present in connection with the occurrence of tapeworm, or other of the diseases referred to, it is to be regarded as a *superadded* but distinct disease. In like manner, an apparent change of chlorosis into pernicious anæmia would be no proof of the relationship of the two. There is no reason whatever why there should not be rarely engrafted upon chlorosis, or upon any other blood affection, or in fact upon any disease whatever, a new condition, a distinct disease, which may chance to be a destruction of red blood-cells. This is very different from the view that has been expressed that pernicious anæmia is a final stage of any other form of anæmia.

Regarding chlorosis, we are believers in the distinctive character of the affection, and view it as in all probability of cytogenic origin—a fault in the proper formation of red blood-cells—as a result of which there is a deficiency in the amount of hæmoglobin present. As there is no evidence of destruction of blood in chlorosis, one is almost forced to the conclusion that it is a disturbance of hæmogenesis, whatever the cause of this disturbance may be.

If one wishes to refuse to pernicious anæmia the title of an independent disease because there may be more than one toxic agent which can act in exactly the same manner and produce similar symptoms, no absolute objection can be made. The disease is secondary in so far as it is hæmolytic. In addition to the absorption of certain ptomaines, it is probable, and reasonable too, that pyrodin and certain other antipyretics, and possibly also other drugs capable of destroying blood, would produce the characteristic symptoms and post-mortem changes, should their action be continuously exerted for some time. It seems better, however, to regard all these cases, including the anæmia seen in atrophy of the gastric tubules and accompanying bothriocephalus latus, as other and different forms of hæmolytic anæmia.

It would then be a just conclusion to regard pernicious anæmia, in the ordinary sense of the term, as a truly independent affection, which may be defined as an extreme and increasing anæmia, without marked loss of flesh, not directly secondary to any anatomical lesion, or to the presence of any parasite, but probably due to the entrance into the portal circulation from the intestine of some certain hæmolytic agent, the origin of which is unknown, but which is possibly of the nature of a ptomaine.

THE CONDITIONS AND PROSPECTS OF THE LIBRARY OF THE SURGEON-GENERAL'S OFFICE, AND OF ITS INDEX CATALOGUE.

By JOHN S. BILLINGS, M.D.,
SURGEON UNITED STATES ARMY.

Of late years those physicians in this country who make use of medical literature in connection with their investigations or writings, have, for the most part, become acquainted with the resources of the "Library of the Surgeon-General's Office," as it is officially designated, and many of them are much interested in its progress and prospects. I am often asked how the collection is progressing, how near it is to completion, what it is most in need of, when the *Index Catalogue* will be done, whether it will be followed by a supplement, whether there is danger that the work of the Library may be checked in the future through changes in administration, and so on. These manifestations of interest are, of course, very gratifying, and when the Chairman of your Programme Committee demanded a ten-minute paper from me on this occasion it occurred to me that I would try to answer some of the foregoing questions so far as I am able to do so.

The present condition of the Library is fairly satisfactory. It now contains 102,000 volumes and 152,000 pamphlets, counting as pamphlets all octavos and smaller sizes having less than 100 pages, and all quartos of less than 50 pages. During the last five years, *i. e.*, from July 1, 1886, to June 30, 1891, the additions to it have included 25,237 volumes and 55,900 pamphlets, or an average of 5000 volumes and nearly 12,000 pamphlets yearly. Of this annual increase, about 2000 volumes and 4000 pamphlets have been of new or current literature, and the remainder have been publications of previous years or centuries. About one-fifth of these accessions, of both new and old literature, have been presented, the remainder have been purchased.

So far as mere size goes, it is the largest collection of medical literature in the world, and for the last five years has been increasing more rapidly than any other similar library containing 25,000 volumes and upward. It is especially rich in medical periodicals and transactions of societies, of which classes it now contains about 34,350 volumes. The American, English, French and German literature in all branches of medicine which has appeared during the present century is very fully represented, and over 90 per cent. of all the medical literature of the world for the last ten years is in the library. The whole is conveniently arranged in a fire-proof building, and is catalogued.

So much for the favorable side of the situation; now for a statement of some of the principal defects and deficiencies. Of medical incunabula, it contains 140 volumes, or about one-eighth of the medical works published prior to 1500. Of the published works of the ancient Greek, Roman, Arab and Hebrew medical authors, it has one or more editions of nearly all, but these editions are not in every instance the best. Of the early Spanish and Portuguese medical literature, it has almost nothing; of French medical works of the sixteenth century, but little; of French medical theses prior to 1800, very few. Of the English, French and German medical books of the 16th, 17th, and 18th centuries, which are of any importance historically or practically, it has about 75 per cent.; of the Italian, about 50 per cent.; and of the Spanish, about 25 per cent. In its periodical literature it is especially deficient in the Spanish and Italian prior to about 1850, in the French prior to 1780, and in the Russian prior to 1860. If I could add to it about ten thousand volumes of my own selection, it would, I think, contain at least one edition of every medical work of any practical use or importance which has ever been published, although it would still not possess some fifty thousand pamphlets and theses, each of which might be of some historical interest.

These deficiencies in the Library are being gradually supplied, but the acquisition of the older books and pamphlets which are still wanted is becoming every year a slower, more difficult, and more costly process. This is due to the fact that the books still wanted are many of them rare, and only appear in the market at intervals of from five to fifty years; to the fact that the number of competitors for such books is increasing, and, above all, to the fact that the

expenditure of time required for the examination of the numerous catalogues and lists received at the Library, in order to select those books which are still wanted, is becoming very great in proportion to the results obtained. To check off a catalogue of a thousand medical books with the result of finding about four which are really desirable, a dozen which may be accepted as filling gaps, and about twenty small theses which are not in the collection, involves an amount of clerical work which costs as much as, if not more than, the books thus obtained. In one sense, it is true that this is a satisfactory condition for a library to be in, but, nevertheless, the time spent in such checking is to be regretted.

With regard to current medical literature, the amount increases each year, but the rate of increase is becoming slower. Comparing the period of 1890 with that of 1880, we find that the number of medical writers increased from 11,600 to about 14,200, or a little over 22 per cent. There were published in 1890 about 2000 volumes and 4000 theses, pamphlets, and reports in medical literature. Of the volumes, about 930, or not quite half, were furnished by medical journals and transactions, as against 864 of the same kind in 1880—being an increase of about 7½ per cent. Excluding the journals, transactions, and theses, the number of medical books and pamphlets published in 1890 was about 1,850 as against 1,600 in 1880—being an increase of about 15½ per cent. This indicates that the increase in the number of medical writers, and in the quantity of medical literature which they have produced, has not been proportionally as great as the increase in population and in the number of physicians in civilized countries during the decade, which confirms the statement which I made ten years ago, that the rate of increase is becoming smaller.

In the United States the proportion of periodical literature to the whole is much greater than it is in other countries—for in 1890 it produced about 250 volumes of medical periodicals, 60 volumes of new medical books, 20 volumes of later editions, and 28 volumes of reprints of English books and transactions; while France produced about 160 volumes of medical periodicals, 250 volumes of new medical books, 20 volumes of later editions, and 15 volumes of transactions; Great Britain about 85 volumes of periodicals, 140 new books, 45 volumes of later editions, and 12 volumes of transactions; and Ger-

many about 175 volumes of medical periodicals, 175 volumes of new books, 80 volumes of later editions, and a dozen volumes of transactions. All this is exclusive of pamphlets. Of course, quantity in medical literature has no definite relations with quality or value, but I am speaking now merely with reference to the number of separate pieces which are to be obtained, catalogued, and cared for, and you will see that including journals, transactions, reports, books, pamphlets, reprints, and theses, we shall have at least 6000 new pieces to provide for this year. The indexing of articles in journals and transactions will involve the writing and classifying of about 25,000 titles in addition.

Of the *Index Catalogue* of the Library, twelve volumes have now been printed—carrying the work to S. The thirteenth volume is nearly ready for the press, and the manuscript for the rest of the work—at least two volumes more—has been prepared, but has not yet been finally corrected and arranged. As we can print but one volume a year, it is evident that during the twelve years which have elapsed since the publication was commenced a large number of titles of books and articles received too late to be placed in their proper places must have accumulated, and this accumulation becomes more rapid every year as we get further down the alphabet in the course of printing the work. At present the number of unprinted titles thus accumulated under authors and subjects down to S, probably amounts to about 70,000 author and 240,000 subject titles, the latter of course including the titles of indexed journal articles. If these were now printed they would make about four volumes of the size of the volumes of the *Index Catalogue*, and three years hence, when this first series of the *Catalogue* is finished, there will probably be material on hand enough to form at least five volumes of a supplement or second series, which will no doubt expand into six volumes by the time the printing of this second series is finished—that is, if the library continues to increase as it has done for the last five years.

The twelve volumes of the *Index Catalogue* already printed contain 137,578 author titles covering 66,855 volumes and 120,000 pamphlets, 522,092 subject titles covering 128,284 titles of books and pamphlets, and 393,808 articles in journals and transactions. The titles of articles in journals and transactions are printed only under subject headings, those of books and separately paged pamph-

lets and reprints are printed twice—once under the name of the author and once under the name of the subject. All the cards for journal articles have been preserved, and when the printing of the *Catalogue* is completed, it is proposed to assort these by authors so as to bring under each man's name the title of all the articles he has written which have been indexed. Whether this will ever be printed I do not know. The chief errors in the *Index Catalogue* are those of omission. About fifty serious errors in the first twelve volumes have thus far been detected, but the main defect is the failure to include under the proper subject headings some books and journal articles which are in the collection. We have gained experience as the work has progressed, and the later volumes seem to be more full and accurate than the first.

Of main and subordinate subject headings the *Index Catalogue*, as a whole, contains about 20,000, and in placing the proper headings on the subject cards to indicate where each is to be placed, it is necessary, in order to secure good results, that the person doing this shall not only remember the general scheme of classification, but the details of between four and five thousand of the subject headings used. If he makes an error, the card goes to the wrong place and is liable to be omitted in printing; but, in the long run, it is sure to be discovered and placed where it belongs.

In connection with the *Index Catalogue* a few words with regard to the *Index Medicus* may be of interest. This, as you know, is in the main a record of the titles of new books and articles in periodicals received at the library, to which are added the titles of a few books advertised as published but not yet received. It is not published by the Government, but by Mr. George S. Davis, of Detroit, who pays all expenses connected with it, and is entitled to the thanks of all who use it for his public spirit and enterprise in maintaining its existence, since the amount received by him for subscriptions barely meets the cost of its publication. At present 482 subscriptions are made for this periodical, of which 90 come from the U. S. Army Medical Department, 224 from the rest of the United States, and 168 from other countries. Of the subscriptions from foreign countries, Australia sends 5; Belgium, 2; Brazil, 1; Canada, 2; England, 41; France, 26; Germany and Austro-Hungary, 63; India, 1; Ireland, 2; Italy, 1; Mexico, 1; Russia, 9; Scotland, 9; Sweden, 2; and Switzerland,

2. Of the home subscribers, California furnished 8; Colorado, 1; Connecticut, 3; District of Columbia, 13; Georgia, 2; Illinois, 9; Kentucky, 1; Louisiana, 3; Maine, 2; Maryland, 10; Massachusetts, 31; Michigan, 8; Missouri, 4; Nebraska, 1; New Jersey, 5; New York, 69; Ohio, 8; Pennsylvania, 33; Rhode Island, 4; South Carolina, 1; Tennessee, 1; Vermont, 1; Virginia, 1; Wisconsin, 4. For the large cities, the figures are, New York, 50; Philadelphia, 32; Boston, 24; Baltimore, 10; Cincinnati, 7; Chicago, 6; San Francisco, 4; Detroit, 4; and St. Louis, 3.

This is the last of the statistics of the Library and matters connected with it which will be inflicted on you at this time. The figures themselves may be dull, but some interesting, and even amusing, conclusions may be drawn from them, which I leave for you to do.

In conclusion, I may say that the future prospects of the Library are excellent. It is not dependent on the skill or energy, or goodwill, of any one man; it is becoming more and more known to, and more and more used by, the members of the medical profession, and so long as they are interested in it, the necessary appropriations will be made and the skilled force employed to increase, preserve, and catalogue it. The service rendered by a number of those employed in the Library is not a mere matter of money—they are deeply interested in their work and proud of the results, and they can and will carry it on and instruct others who will come after them and do likewise. They have to handle much rubbish, for the proportion of what is both new and true is not much greater in medicine than it is in theology, but in a great national collection this is unavoidable, and the best they can do is to make a first rough assortment, and then make the whole accessible to those who wish to use it. There is no doubt that the publication of the *Index Catalogue* will be completed, nor that a supplement will speedily follow.

Just at present the most unsatisfactory thing about the Library is the fact that many of its books and journals are not fully available for use owing to the fact that we cannot get them bound. Under existing laws all the binding of the Library must be done at the Government Printing Office, which has not room nor men sufficient to do the work required for the different departments of the Government and for members of Congress. The result is that the Library now has about 10,000 unbound volumes, and this number is increasing every

year. When a journal is sent to be bound it may be six months or more before it is returned. With the erection of additional accommodations for the Government Printing Office it is to be hoped that this evil will in time be abated; but there will always be more or less delay in making recent books and periodicals available for use under the present system. The most effectual remedy would be a change in the law, whereby the Library could have its own binding done in its own building and under its own control.

DISCUSSION.

DR. W. T. GAIRDNER, of Glasgow: The first time I heard of Dr. Billings and his magnificent labor was when he made a sudden appearance in Glasgow, I am afraid to think how many years ago, and put himself in communication with Finlayson and myself. He had a ravenous appetite for anything in the way of printed matter that was likely to escape his attention. Dr. Finlayson, being Librarian to the Faculty of Physicians and Surgeons, was in a position to do a great deal for him; I was able to do much less, but still a little. The consequence was that we sent Dr. Billings off with an enormous amount of "rubbish" swept up from the dust-bins—all that could possibly be carried off by one man. We could not see how this mass of rubbish could be reduced to order, but a few years later we got the first volume of that magnificent *Index Catalogue*. There we could see that the genius of Dr. Billings had mastered this mass—a mass inscrutable so far as Glasgow was concerned—and had reduced it to the order now described. I do not think this has ever been done before—certainly never before in medicine—and I very much doubt if it has ever been done in any other department of human thought.

On various occasions it has happened to me, upon becoming interested in some particular subject, to find out from Dr. Billings's catalogue that I had written something on the subject twenty years before which had entirely escaped my memory.

For people who will speak on every occasion about the things they know and the things they do not know, it may be a very terrible thing to be confronted suddenly with an extract out of Dr. Billings's catalogue with a reference to a paper which shows that a man has said something utterly contradictory to something he is saying now, with the presumption that he knew just as much about it when he said the one thing as when he said the other.

I would not willingly sit down without seriously saying that there is no work of the present generation that strikes me more with the idea of the stupendous, and also as being animated throughout by the qualities amounting to genius, than that magnificent catalogue.

A CASE OF SLOW PULSE.

By D. W. PRENTISS, M.D.,
OF WASHINGTON, D. C.

WITH THE REPORT OF THE AUTOPSY.

By ROBERT T. EDES, M.D.,
OF WASHINGTON, D. C.

THIS report is to complete the case of "Slow Pulse" previously read before this Association and published in its *Transactions* for 1889 and 1890. The members may remember that the patient was brought before them for examination, both last year and the year before. He has since died, and this statement, with the report of the autopsy by Dr. Edes, completes the case.

This man, aged fifty-three years, had a pulse ranging from 11 per minute to 40 per minute for over two years, being subject to frequent attacks of syncope. No disease of heart or other organs could be discovered.

The following is the record since last report (May, 1890):

	Pulse.	Temperature.	
May 20, 1890.	—	——	Became worse; dizzy.
24,	13	97°	Fainting spells almost constant; tightness across chest; no pain; bromide of ammonia; stimulants; morphine and atropine as necessary.
26,	14	—	Only slight spells.
30,	18	——	Only slight spells.
June 10,	34	100°	Great many spells; has fallen twice, once cutting his head.
12,	15	——	
14,	16	——	Pulse irregular; diarrhœa.
19,	16	——	Few spells; fell.
29,	21	——	More or less delirious for several days.
July 2,	15	——	Delirious; restless; wanders about house; afraid of being killed.
4,	—	——	Died at 6 P.M.

Had been more delirious and excited than usual; thought several persons were trying to kill him. Rushed about the house, screaming in terror—"Murder! Fire!" etc., until the neighborhood was aroused. Was finally induced to lie down, and seemed quiet. His wife left him for a few moments and on returning found him dead.

Autopsy, Seventeen Hours After Death.

Expression tranquil. Body tolerably well-nourished; considerable fat under the skin and in cavities. Very little hypostatic congestion. Blood everywhere dark and fluid, except a few small, loose, black clots.

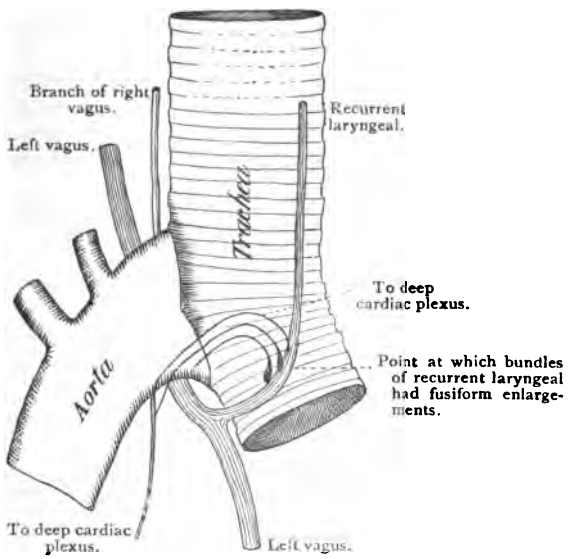
Lungs posteriorly, moderately congested, crepitant. No fluid in pleuræ pericardium, or peritoneum.

Heart rather large and firm. Lungs being well dilated, it is probable that no more than the normal surface of the heart came in contact with the thoracic wall. Neither the aorta nor the coronary arteries were atheromatous.

Stomach normal; intestines not opened.

Spleen moderately firm, medium size.

Kidneys congested, capsules not adherent. No atrophy. Healthy.



Aorta lifted up to loop of recurrent laryngeal.

Brain and upper portion of spinal cord healthy to gross appearance. On the right side, the upper cervical ganglion of the sympathetic, the lower cervical ganglion, a portion of the thoracic sympathetic, a portion of the splanchnic at semilunar ganglion were removed. On the left side the same

portions, except the upper ganglion and the thoracic sympathetic. All these appeared normal to the naked eye.

On dissection of the heart, the left pneumogastric appeared normal until the region was reached where it bends under the arch of the aorta to give off the recurrent laryngeal. Here several of the strands appeared somewhat less clearly defined through the surrounding connective tissue, which, at this point, was more strongly adherent. There were fusiform enlargements of the several cords. One of these was on a cord going downward to form the œsophageal plexus; others were on the bend of the recurrent laryngeal just below the artery. At this point the recurrent laryngeal gives off branches which connect with the cardiac plexuses. The muscular substance of the heart was firm and not fatty. Walls of both ventricles thickened, those of the right perhaps more in proportion to its usual thickness. (See diagram.)

The various portions of the nervous system above mentioned were examined microscopically after hardening in osmic acid.

The fusiform enlargements at the point of separation of the cardiac branches from the recurrent laryngeal were so much dragged upon and injured in the process of dissection, that the microscopic examination was entirely unsatisfactory and disclosed nothing. The other cords and ganglia, including portions of the cardiac plexuses, showed no increase of connective tissue nor any atrophy either of nerve-fibres or ganglionic cells.

The intrinsic cardiac ganglia I failed to find.

Sections of the medulla were made and stained. Here also the hardening had not been entirely successful, but fortunately the sections at the level of the pneumogastric nucleus were sufficiently good to show that there was no lesion at this suspected point. The most that could be said of the medulla as a whole, was that it appeared to be congested.

I am much indebted to Dr. Gray, of the Army Medical Museum, for sections of the upper part of the medulla oblongata.

DISCUSSION.

DR. PEPPER: This report of Dr. Edes, it seems to me, may be considered as a negative report.

DR. EDES: I think the point of finding those enlargements renders it not entirely negative.

DR. PEPPER: Were there lesions of the nerves at those enlargements?

DR. EDES: It seemed to me that there was increase of the connective tissue at that point.

DR. PEPPER: The condition of the nerve was not materially different from the adjacent portions?

DR. EDES: That I could not say, because the parts were too much injured to show this exactly.

DR. PEPPER: I have refreshed my memory in regard to the discussion on this case last year. Nearly all the speakers thought the patient was the subject of arterio-sclerosis. The radials were hard and evinced an increased tension. But I gather from the report that there were no material changes in the coats of the arteries.

DR. WELCH: It would be interesting to know whether Dr. Edes has made comparison with the condition of the cardiac nerves in normal subjects. It occurs to me that possibly the fusiform enlargements, which he mentions as the only observed change in the cardiac nerves, may correspond to ganglionic swellings, which are somewhat variable in their size and position on the cardiac nerves. One sometimes finds instead of one ganglion in its usual position, a series of smaller, scattered nodules giving more or less of a varicose appearance to the nerve. A microscopic examination would, of course, have settled the question.

EXHIBITION OF SPECIMENS OF HAIR SHOWING DISCOLORATION FROM INTERNAL USE OF PILOCARPINE AND JABORANDI.

By D. W. PRENTISS, M.D.,
OF WASHINGTON, D. C.

THE first case was that of a young lady who up to twenty-five years of age had light blonde hair. She was treated with hypodermic injections of pilocarpine, one-sixth of a grain two or three times a week, for uræmia from suppression of urine. In two weeks' time her hair was distinctly brown, and in six weeks it was black. This was ten years ago; the color of her hair at this time is still black.

Another case was that of an old lady suffering from interstitial nephritis; her hair was quite white. The principal symptom which gave her distress was itching of the skin from dryness. For relief of this, fluid extract of jaborandi was given. This gave relief for nearly a year. In the course of eight or nine months it was noticed that her eyebrows were black, and after that her hair in patches over her head became black, and there was new hair growing all over the scalp. Before this growth became of any length she died.

ON CHANGES IN THE RED BLOOD-CORPUSCLES IN THE PERNICIOUS ANÆMIA OF TEXAS CATTLE FEVER.

By THEOBALD SMITH, Ph.B., M.D.,
of Washington, D. C.

(From the Pathological Laboratory of the Bureau of Animal Industry, Department of Agriculture, Washington, D. C.)

Texas fever among cattle is a disease peculiar in this, that it is conveyed by healthy animals from a definite geographical region to those living north of this region.

In 1888 I enjoyed the first opportunity of examining several of the internal organs of five animals which had succumbed to this disease. I was at that time struck with the similarity between the lesions of this disease and those produced by various observers in smaller animals by the injection of substances which break up red blood-corpuscles. These lesions were, in brief, engorged spleen, injection of the bile capillaries with solid bile and fatty degeneration of the liver cells, very thick, flaky bile in the gall-bladder, and hæmoglobin in the urine. While these phenomena might be interpreted equally well according to several widely different hypotheses, I was led to assume a destruction of the red corpuscles by an intra-globular parasite, for which malaria in man and the hæmoglobinuria of cattle in Roumania offered some points of support. In the first fatal case which permitted an examination of the blood in the various organs, and which came into my hands the following summer, a parasite was found. These earliest observations are published in a very brief form in *The Medical News* of December 21, 1889. This parasite has not been missed in any of the numerous cases which have been examined since that time, nor has it been detected in the blood of cattle during health.

During the course of the investigation there appeared in certain cases

a peculiar condition of the blood corpuscles which I was inclined to consider a result of the anæmia, but which might have passed for a stage of the intra-globular parasite. In resolving the doubts concerning these corpuscles, I was led to the observations embodied in this communication. They were made on at least sixty cases of the disease, and controlled by many examinations of healthy animals. They are but indirectly connected with the etiology, which I purposely avoid discussing until all the experimental evidence shall have been published together.

The destruction of red corpuscles, as pointed out in 1889, is the primary factor in the production of the various lesions of Texas fever. As illustrations I may cite the following cases:

I.

August	22, 1890	. . .	7.3 million	red	corpuscles	in a c.mm.
"	23, "	. . .	7.0	"	"	"
"	25, "	. . .	4.1	"	"	"
"	27, "	. . .	3.0	"	"	"
September	11, "	. . .	3.2	"	"	"
"	20, "	. . .	4.5	"	"	"

Recovery.

II.

August	21, 1890	. . .	4.8 million	red	corpuscles	in a c.mm.
"	22, "	. . .	3.5	"	"	"
"	23, "	. . .	3.1	"	"	"
"	27, "	. . .	3.0	"	"	"
September	4, "	. . .	2.2	"	"	"
"	12, "	. . .	3.8	"	"	"
"	18, "	. . .	4.4	"	"	"

Followed by relapse and final recovery.

III.

August	12, 1890	. . .	6.0 million	red	corpuscles	in a c.mm.
"	15, "	. . .	4.6	"	"	"
"	23, "	. . .	2.9	"	"	"

September 3—dies.

A glance at these tables shows how enormous this destruction of red corpuscles must be. One million in a c.mm. a day, or about one-sixth of the normal number, is not an uncommon occurrence in acute fatal cases. In mild attacks leading to recovery the number disappearing each day is much smaller, as I shall be able to show in another

table. That there must be profound disturbance of the organs engaged in the production of red corpuscles is very evident. These disturbances are manifested primarily in the corpuscles sent out to supply the place of those destroyed. In order to make clear what changes have been actually observed, it is desirable to give briefly the methods by which they are made manifest.

The blood coming from a small incision through the previously shaved skin was transferred as rapidly as possible to a slide with a looped platinum wire and covered with a cover-glass. The margins of the latter were sealed with melted paraffin applied with a camel's-hair brush. Various diluents were found unsatisfactory and unnecessary. Thus, salt solution tried in strengths of 0.6–0.8 per cent. swelled up the corpuscles so that what was at first visible within them soon disappeared from view. Iodized amniotic fluid from cattle was found very useful in diluting the blood of the parenchyma of various internal organs.

In preparing dried films according to Ehrlich's method the blood was collected in the same manner. A drop was placed on a cover-glass held between the fingers of the left hand, and one edge of a square cover held with the fingers of the right hand at an angle of about 30 degrees to the first was moved over the latter, causing a rapid distribution of the blood and speedy drying. By this process the corpuscles are not distributed in a uniform layer over the cover-glass, but the layer shades from a very thin to a dense one. In the thinnest portions formed first by the edge of the moving cover-glass the corpuscles are far apart and perfectly preserved. As the layer grows in density the drying is somewhat retarded. This variation in the film is not only no disadvantage, but a positive advantage, for it furnishes a series of forms not all fixed alike. Moreover, in hunting for modified corpuscles, the thicker portion of the film frequently reveals them very soon, though they may have been searched for in vain elsewhere. The conditions under which such films are prepared with most success are not easily ascertained. Besides the state of the blood itself, the relative humidity and the temperature of the surrounding air in hastening or retarding the drying seem to have much to do with it. I cannot attribute any deleterious influence to the moisture given off from the fingers. The success in any case depends largely on the rapidity with which the preparation is made. The method generally recommended

of allowing the blood to spread out between two cover-glasses and then drawing them apart I tried at first, but gave it up for the one described. A speck of dust on either cover prevents them from adhering and jeopardizes both preparations. Even with the greatest care dust is apt to appear on the glasses just before use.[1]

In staining the intra-globular body Löffler's alkaline methylene-blue has given very satisfactory results, and hence the changes observed in the red corpuscles were detected with this stain. To obtain comparative results it has been adhered to more or less throughout. The thoroughly dry film of blood or tissue may be fixed in several different ways, all well known to most of you: 1. For rapid work the cover-glass may be drawn through the flame of a Bunsen burner four times. It should be moved through a distance of about five inches—*i. e.*, two inches each side of the flame. Each single movement should occupy about a second. If only three excursions through the flame are made, the hæmoglobin may dissolve out during the staining process. 2. The cover-glass is kept in a dry chamber at 110°–120° C. for one or two hours. 3. It may be placed in a mixture of equal parts of absolute alcohol and ether for several hours. The second method is safer than the first, and should be employed whenever possible.

Films fixed according to any of these ways are stained for a few minutes in alkaline methylene-blue, washed in water, then dipped for from one to two seconds in a 0.3 to 0.5 per cent. solution of acetic acid, to remove the diffuse stain. This decolorizing is very important as a means of differentiation when the above stain is used, and must be carefully done. The preparation is again washed in water and may be examined at once, or permanently mounted in xylol balsam. Simple watery solutions of methylene-blue, though they bring out the same features, do so much less distinctly, and after a much longer exposure. By using them we may dispense with the subsequent use of acids, however.

The blood of cattle in health contains on an average from 5.5 to 6.5 million corpuscles in a c.mm. They are somewhat smaller than

[1] Occasionally cover-glasses show the presence of a film of grease even after prolonged stay in cleaning solutions. Drawing them through the flame, each surface twice, removes all tendency of the drop of liquid to remain massed together.

those of man, and vary in diameter from 4 μ to 6 μ.[1] If in the disease before us, we direct our attention to preparations of fresh blood, we find that a reduction of their number to 3 million does not lead to any changes excepting a slight increase in size of a small percentage. As the number continues to fall from this point, the tendency to grow larger affects a greater number of cells. When recovery ensues, the number of enlarged corpuscles or macrocytes grows with the increase in numbers, as a whole, up to a certain point, which may be fixed at about 3 million. They remain as such in the circulation until the 4 million point has been passed. The diameter of these macrocytes varies from 6 μ to 8 μ. Not infrequently some measure 10 μ.

More than increase in size is not noticed in fresh blood, except when the number has reached a minimum compatible with life under the conditions imposed by the disease. This minimum rarely falls below one million. Then the largest cells no longer present a homogeneous appearance, but are faintly granular and the hæmoglobin tint is not very pronounced. Under ordinary conditions they do not seem to lose their circular form more rapidly than the smaller corpuscles in the same blood. There is, however, a strong tendency toward changes of form in all the corpuscles of anæmic blood after it is drawn, which may correspond to the poikilocytosis of pathologists. Several times when the lens accidentally pressed upon the cover-glass very *bizarre* forms were produced, quite like those pictured in text-books as poikilocytes. Microcytes, or very small corpuscles, were not present in appreciable numbers in any stage of the anæmia, the tendency being wholly the other way. In but one case of extreme, fatal anæmia I noticed that the corpuscles had not increased in size.

In blood from cases of advanced anæmia, kept sealed with paraffin and examined immediately or after sixteen or twenty hours, the largest corpuscles were observed to be vacuolated. A clear, circular space, about 2 μ in diameter, had formed somewhat excentrically, and might have been confounded with the Texas fever parasite in the spherical state which it assumes after the death of its host. But this parasite is never found in these modified corpuscles. Moreover,

[1] No attention has been paid to the leucocyte elements, since they do not appear to be affected by this disease to any marked degree, either as to kind or number.

within the vacuole in most cases a dark particle, barely visible at a thousand diameters, was seen in a state of violent agitation.

When a series of preparations of blood from cases of progressive anæmia are fixed and stained in the manner described, certain peculiar conditions of the enlarged corpuscles may be noted. When the number has fallen slightly below 3 million, a small percentage appear with a variable number of stained particles disseminated uniformly through the corpuscle. In some cells these particles are relatively large, many attain a diameter of 0.5 μ, and then appear strikingly like micrococci if it were not for a certain variability in size. Each corpuscle may contain from five to twenty or more of these bodies. To those who for the first time examine a stained film of such blood, they are quite puzzling. In the more crowded areas of the film, groups of coccus-like bodies appear everywhere, each group representing the disc of some enlarged corpuscle, the outlines of which are, as a rule, not distinct in such situations. As the number of cells continues to fall, corpuscles appear which are beset with an increasing number of stained particles, diminishing in size until forms appear the disc of which seems covered with a precipitate of exceedingly minute stained points. Not all the particles with recognizable form are round, coccus-like, but some are angular and some appear like very short rods. As a rule, the smallest particles are associated with the more advanced stages of anæmia, although cells with the granules of various sizes are found together.

When the number of corpuscles has descended to between 1.5 and 2 millions, a still further modification appears. Many of the large corpuscles now retain a uniform and pronounced bluish-red color after staining. Such corpuscles are usually somewhat folded, owing to their thinness. The edges are not sharply defined and within the disc there is sometimes a paler, circular or elongated spot from $2\frac{1}{2}\,\mu$ to 3μ in diameter. The stain is not resolved into points by high powers ($\times$ 1500). Curiously enough, corpuscles containing stained granules have not been detected in preparations from the parenchyma of spleen, liver, and kidneys. They are evidently confined to the circulating blood. Diffusely stained cells are not so restricted, but may be observed in the organs as well.

In blood containing from 1 to 2 million corpuscles, nucleated red corpuscles or hæmatoblasts are present. They increase in number as

the whole number of corpuscles diminishes. Thus in blood containing 2 millions they are detected with some difficulty. When the number has fallen to 1 million about 5 per cent. are present. In several instances opportunity was afforded of observing the distribution of hæmatoblasts. In such cases they were equally abundant in the circulating blood, in the spleen, the liver, and the kidneys. The spleen thus did not appear to have undertaken any blood-forming function.

The order in which these different kinds of corpuscles appear in the circulation, as well as the particular stage during which each kind makes its appearance is, as might be expected, not always as described above, although the description given applies to the great majority of cases examined. In those animals in which the destruction goes on very rapidly, fully two-thirds of all corpuscles may have been destroyed before any of the modifications appear, and in most acute fatal cases death ensues before they are observed at all. It is only in the more chronic, milder cases that these modifications are best studied. Their disappearance, when recovery begins, is in the inverse order of their appearance and goes on quite rapidly.

IV.—Artificial Reduction of Red Blood-corpuscles in a Cow.

The operations were performed for me by Veterinarian F. L. Kilborne, assisted by E. C. Schroeder.

Date.	Number of corpuscles in millions in a c.mm.	Quantity of blood withdrawn. (Jugulars.)	Remarks.
Aug. 3, 1891	6.75[1]	2.268 kgr.	Blood elements not visibly changed.
" 4, "	5	2.325 "	" " " " "
" 5, "	4.65	.....	" " " " "
" 6, "	5.22	3.827 kgr.	" " " " "
" 7, "	3.82	4.251 "	" " " " "
" 8, "	3.09	4.989 "	2 to 3 per cent. show stained granules; about 10 per cent. appear enlarged.
" 10, "	2.25	.....	20 per cent. of macrocytes; 15 per cent. contain stainable matter chiefly as granules.
" 11, "	2.14	.....	Same as yesterday.
" 12, "	2.11	.....	Same as yesterday; one hæmatoblast seen.
" 14, "	2.53	.....	Numerous macrocytes; about 5 per cent. contain stained particles.
" 17, "	3.2	.....	Macrocytes as before; cells with granules rare.
" 22, "	3.2	....	Macrocytes as before; no stained granules detected.
" 29, "	4.3	.....	Only a few macrocytes.

[1] The number of corpuscles determined each day before blood was withdrawn. The percentages are mere approximations made from dried and stained films.

V.—MILD ATTACK OF TEXAS FEVER.

Date.	Corpuscles.	Remarks.
Dec. 22, 1890	5.57 million	Blood corpuscles normal.
" 27, "	5.07 "	" " "
Jan. 16, 1891	4.38 "	Blood corpuscles normal in form; 15 to 20 per cent. of infected corpuscles.
" 20, "	3.07 "	Same condition as at preceding examination.
" 22, "	3 "	Some macrocytes; 5 to 10 per cent. of corpuscles with stained granules; about 1 per cent. diffusely stained; about 20 per cent. of infected corpuscles.
" 24, "	1.92 "	Abnormal forms increased in number; several hæmatoblasts. Same number of infected corpuscles.
" 27, "	1.25 "	Many macrocytes; about 20 per cent. of all cells with stained granules or tinted disc; 5 per cent. hæmatoblasts; about 10 per cent. of infected corpuscles present.
" 29, "	1.26 "	Same as before. Infected corpuscles diminished to about 5 per cent. Vacuoles (?) in largest macrocytes.
" 31, "	1.45 "	Same as at preceding examinations.
Feb. 5, "	2.36 "	Many macrocytes; several hæmatoblasts; only 1 to 2 per cent. of corpuscles with stained granules; infected corpuscles rare.
" 9, "	2.68 "	Macrocytes as before; granular cells scarce; 2 to 3 per cent. of infected corpuscles.
" 12, "	3.1 "	Macrocytes as before; granular cells scarce; one hæmatoblast seen; 1 to 2 per cent. of infected corpuscles.
" 18, "	3.27 "	Same as on February 12th; infected corpuscles rare.
" 26, "	3.7 "	A few macrocytes.
Mar. 10, "	4.26 "	Macrocytes rare.
" 18, "	5.31 "	Corpuscles normal.

That these morphological variations are due to the anæmia and not to any other cause may be demonstrated by practising venesection on healthy animals. They were called forth both in a cow and in a lamb by artificially reducing the number of red corpuscles by blood-letting. The preceding figures, taken from two cases, illustrate the various statements made above.

We have now seen that in the progressive anæmia of the ox or sheep due to disease or loss of blood there appear in the circulation: 1, enlarged red corpuscles (macro- and megalocytes); 2, enlarged corpuscles in which granules may be detected by nuclear stains; 3, enlarged corpuscles which stain diffusely, and 4, nucleated red corpuscles or hæmatoblasts.

We shall not be far from the truth, I think, in assuming that we have here unfinished or embryonic corpuscles, sent into the circulation before their time to make good the losses going on. We are led from the enlarged but otherwise normal corpuscle through those containing

granules and staining diffusely to the hæmatoblast. Each stage is more embryonic than the preceding and called into active service by more and more pressing need.[1] We are, however, justified in asking whether these stages are those which the corpuscles ordinarily pass through, or whether pathological conditions are superadded. It is highly probable that there is both an embryological and a pathological factor involved. As an illustration of the former, I may cite the following observation.

Recently I had the good fortune of examining the blood of a fœtus, three months old, taken from a cow which had succumbed quite suddenly to Texas fever. This blood, with its large corpuscles and occasional hæmatoblasts, resembled markedly the blood in Texas fever, or after severe bleeding. The resemblance was still more striking when dried films were stained. A considerable number of corpuscles became diffusely colored, just as in advanced stages of anæmia in the adult. Cells with granules were not observed. There was no reason for supposing the blood of this fœtus diseased, as it was not infected with blood parasites, and the mother had succumbed so quickly that even in her blood no embryonic forms were as yet present.[2]

The particles and granules within the embryonic red corpuscles behave like nuclear substance. They take up basic aniline colors and hæmatoxylin. Methyl-green in watery solution failed to stain them. I at first regarded them as remnants of the nucleus. But this theory was abandoned when they were found in hæmatoblasts themselves. The embryonic corpuscles which become diffusely stained contain a substance which behaves as the granules do. It is highly probable that this substance is protoplasm incompletely transformed into the cell contents of the adult red corpuscle, and that the granules are derived from it in the circulating blood by a drawing together or condensation of it. We may look upon these granules as the pathological element perhaps of the transition forms produced by a premature assumption of the respiratory function.[3] . We have already seen that they are not found in the organs nor in embryonic life.

[1] Very significant is the fact that these modified or embryonic forms are not infected. Only the adult forms meet this fate.

[2] I have observed red corpuscles which retain a bluish-red color after staining with methylene-blue in guinea-pigs, rabbits, rats, mice, and pigeons kept in cages. The proportion of these transition-forms varied considerably in the different species. I have never observed them in healthy cattle.

[3] I have no data concerning the fate of these transition forms in the circulation.

So far as I have been able to ascertain, W. Erb[1] was the first to call attention to granules in red corpuscles, not only in animals upon which repeated venesection had been practised, but also in human patients after severe hemorrhages and during chronic disease. He even found them in certain animals, such as rabbits, dogs, rats, young cats, and calves, quite constantly under ordinary conditions of life. Such corpuscles were larger than normal ones. The granules were not detected in fresh blood until treated with 1 per cent. acetic acid or with picric acid. In man, according to his observations, from two to four days elapsed after a hemorrhage before the transition forms began to appear.

How far the granules described by Erb are identical with those observed by me I am unable to state, since I have not succeeded in bringing them out with acetic acid, either in the fresh or the dried blood.

Löwit[2] observed granulations in red corpuscles of the rabbit when fresh blood from certain vascular territories was treated with a modified Pacini's fluid. These he regarded as the remains of a nucleus.

Howell[3] calls attention to granules brought out by methyl-green in the hæmatoblasts of cats severely bled, which may be identical with those in the blood of cattle and sheep.

Granules within red corpuscles which stain deeply with methylene-blue have been observed by Celli and Guarnieri.[4] They also call attention to punctiform or streaked staining either near the centre of the corpuscle or scattered through it. The same authors briefly mention Foá and Mondino as having demonstrated similar bodies and referred them to remains of a nucleus. Observations on man which most nearly accord with my own on the ox, both as regards the method employed and the results obtained, are those of Ehrlich and Gabritschewsky. Ehrlich in the *Charité Annalen* for 1885 very briefly mentions the important fact that in anæmic blood certain red corpuscles become stained with hæmatoxylin and with methylene-blue. He was also able to demonstrate granules within the blood corpuscles with the last-named dye. According to the same author Favre and Celli

[1] Archiv f. path. Anat., Bd. xxxiv., 1865, S. 138.
[2] Sitzungsbericht d. k. Akad. d. Wiss., Bd. xcv., 1887, S. 144.
[3] Journ. of Morphology, iv., 1890, p. 85.
[4] Fortschritte der Medicin, 1889, S. 521.

detected similar appearances in malarial blood. Ehrlich looked upon this condition revealed by stains as a progressive coagulation-necrosis of the stroma, or discoplasma, as he is inclined to call it.

Gabritschewsky,[1] in a recent publication, gives a history of five cases, in all of which he found the diffusely stained corpuscles after applying practically the same method (Ehrlich) which has been described in detail above. Two of the cases were affected with leukæmia, and in four out of five a greater or smaller reduction in the number of red corpuscles was noted. Cells containing granules were not seen. My own observations thus accord entirely with his as far as the latter have gone. He likewise rejects Ehrlich's interpretation that such forms are degenerated corpuscles, and suggests that they may be corpuscles the development of which has been arrested at a certain stage. .

Attention has already been called to nucleated red corpuscles in the blood when the latter contains between one and two million corpuscles. These cells are naturally of great interest, as they are most likely the progenitors of red corpuscles. I feel no hesitation in affirming that they are the progenitors, at least of the enlarged and modified corpuscles which have been described. In the marrow the large corpuscles or megalocytes were identical in appearance and size with those still containing a nucleus. In the circulation the youngest red corpuscles were made up of the same stainable protoplasm which characterized the hæmatoblasts.[2] The latter in several cases contained the same granules found in the red corpuscles. In short, everything pointed to the hæmatoblasts as their ancestors.

While I believe this view is held by most authorities to-day, and I simply state the observations as strengthening that view, the problem concerning the manner in which the hæmatoblasts rid themselves of their nucleus is not yet near solution. My own somewhat desultory observations inclined me at times to the theory that the nucleus disappears within the corpuscle, but all such observations were after a time found to point the other way—namely, that the nucleus leaves the cell.

In two cases I observed in the marrow almost every hæmatoblast with more than one nucleus. The greater number contained two, the

[1] Archiv f. exp. Pathologie und Pharmakologie, 1890, xxviii. S. 83.

[2] This fact was noted by Gabritschewsky in the article quoted above.

remainder from three to five. These observations were made on fresh marrow in iodized serum. Films dried and stained cannot be utilized for this purpose. Rarely hæmatoblasts with two nuclei were detected in the circulating blood. As they approach maturity the nucleus becomes smaller and more compact, and stains solidly and deeply with methylene-blue. This fact could be observed in the marrow of all cases examined, of which there were fifteen. It was likewise noted in the circulating blood of one case in which hæmatoblasts were fairly abundant. As to the actual extrusion of the nucleus, only the following facts came under my observation. In several cases of extreme anæmia I saw among the hæmatoblasts in blood just drawn and examined fresh in the paraffined cell a small number with partly extruded nucleus. In several instances the latter was constricted, the corpuscle clasping it around the constricted portion. A few were detected with wholly external but adherent nucleus. In the marrow only very rarely partly extruded nuclei were seen. In one stained preparation of blood I noticed a large diffusely stained corpuscle with two small nuclear fragments imbedded in its centre, as if the nucleus had broken away in fragments. In large corpuscles, evidently embryonic, I noticed in fresh preparations at times a small heap of granules somewhat excentrically situated. These were also observed in the fœtal calf referred to above, and at first interpreted as a disintegrated nucleus until I observed the same thing in those still containing the nucleus.

It is obviously hazardous to endeavor to group these isolated observations under any hypothesis. But it seems to me possible to explain them by the following assumptions: In case of a sudden loss of blood, the hæmatoblasts multiply in the marrow by indirect division. This may go on to a certain extent until the nucleus shrinks, becomes smaller, and presents an intensely blue appearance after staining with methylene-blue. In this condition, I believe, the nucleus simply breaks away from the cell-body; active emigration may take place, but only under abnormal conditions. In one case the blood contained both mature and immature hæmatoblasts. And, curiously enough, only the nuclei of the immature ones were in a state of partial extrusion, while the mature ones were situated within the cell. The relative maturity of these hæmatoblasts is easily determined by the appearance of the cell-body. The immature forms stain uniformly; the mature

forms stain not at all, and may exhibit a small number or stained granules. It should be stated that this view agrees, in the main, with that of Howell, with the exception that in the one just stated the extrusion of the nucleus is regarded as a passive process—a mere casting off. How truly this shedding of the nucleus, so to speak, represents the actual occurrence, must be determined by additional carefully directed investigations. Meanwhile, it best explains the appearances which I have met with.

The occurrence of very large corpuscles (megalocytes) in cases of extreme anæmia is a phenomenon deserving some attention. When the number has fallen to a certain low point, and their destruction still goes on, the new elements which appear in the circulation grow, in certain cases, gradually larger in diameter. This may be due to a lack of those elements (erythroblasts of Löwit) which develop into red corpuscles, and hence each one is somehow stimulated to an over-production of corpuscular matter. While this explanation is supported by the researches of Laache,[1] that the large corpuscles contain more hæmoglobin than the normal forms, it can hardly be considered as applying to all cases. It is a matter of observation that the larger the corpuscles become, the thinner and more delicate they are and the less hæmoglobin they appear to contain. Their bulk, as a whole, does not seem to exceed that of the thicker normal cells. In short, they are nothing more than embryonic forms. In those cases, on the other hand, in which an over-production of discoplasma seems to take place, the difficulty may rest with the nucleus. If the fresh supply of corpuscles is, as seems highly probable, due to division of the hæmatoblasts into two or more cells, this power of reproduction may come to an end, and then each nucleus might form around it the protoplasm belonging to two or more cells, thus giving rise to the megaloblasts and gigantoblasts of authors.

In this connection it is pertinent to mention a recent article by Rindfleisch[2] in which he called attention to the condition of the marrow in a case of uncomplicated pernicious anæmia. In it the number of nucleated corpuscles or hæmatoblasts was very great while he colorless corpuscles were present in small numbers. The former

[1] Die Anämie. Christiania, 1883.
[2] Arch. f. path. Anat., cxxi. S. 176.

were remarkable for their large size, some having a diameter of 50 μ. Rindfleisch infers that the trouble in this case lay in a retardation of the emigration of the nuclei. This, he thinks, would explain the anæmia and account for the increase in size of the hæmatoblasts, whose growth was abnormally prolonged. It seems to me that in this case the enlarged condition of the hæmatoblasts may be explained as the result of a too great demand made upon them and their progenitors by some previous, unnoticed loss of blood and that it is not due to any fault inherent in the hæmatopoietic function. The theory of Rindfleisch should demand the free entrance of hæmatoblasts into the circulation. Unfortunately the blood was not examined during life, and after death the right ventricle contained macrocytes and poikilocytes, but no hæmatoblasts.

By the same reasoning other pathological states of the blood elements referred to various primary causes may be conceived of as the result of some sudden and severe, or mild and prolonged strain on the blood-forming function in the past, from which the system never fully recovered.

It is evident that the recognition of embryonic or unfinished corpuscles in the blood may beof considerable clinical value, and may be utilized in a number of ways which will readily suggest themselves to such as are interested in the study of the blood. Ehrlich and Gabritschewsky have made us acquainted with such corpuscles in human blood, and the latter has correctly interpreted them. The abundant material from which I have been able to draw the same conclusions will, I think, completely set aside the view of Ehrlich, that they are primarily degenerate forms. That they must have been frequently observed in human blood I do not doubt, but an occasional red corpuscle which stains diffusely among a large number which do not is likely to be regarded as an accident of the mode of preparation and its real significance overlooked.[1]

[1] My own experience with human blood is limited to a single case, but is worth mentioning here. In January, 1890, through the courtesy of Dr. D. W. Prentiss I was enabled to examine the blood of a case of purpura. In it I found a small number of diffusely stained corpuscles and I at once diagnosed them as newly-formed corpuscles in accordance with my experience with Texas-fever blood. The history of this case was presented to this Association by Dr. Prentiss in May, 1890, with my diagnosis of these stained corpuscles. This, therefore, antedates Gabritschewsky's paper.

What has been determined concerning embryonic corpuscles in Texas-fever blood may be briefly formulated as follows:

1. In an acute attack, the number of corpuscles may fall so rapidly that the low figure of two millions may be touched before any transition forms appear. It should be borne in mind that the great derangement of the functions of the body due to such enormous destruction of corpuscles retards their regeneration.

2. Transition forms (macrocytes, corpuscles with granules and diffusely stained, and hæmatoblasts) appear most promptly in mild cases of Texas fever and after severe loss of blood in otherwise healthy animals. They disappear equally fast when the number of corpuscles again begins to rise.

3. When the anæmia has lasted for a certain time and becomes stationary, as it were, transition forms may be almost entirely absent.

4. The presence of these forms, when there is suspicion of infection and no history of any very severe hemorrhage, is almost as certain a diagnostic sign as the parasite itself. It is possible to estimate approximately, from the number and kinds of transition forms, the number of corpuscles still in the blood and the time which had elapsed since their destruction began. The presence of these forms is a favorable sign and may serve, when taken into consideration with the parasite, as a fairly good basis for a prognosis.

In conclusion, I wish to acknowledge the constant assistance of Dr. F. L. Kilborne, in the collection of the blood, and of Dr. E. C. Schroeder, who has relieved me of the laborious work of counting corpuscles during the present and the past summer.

DISCUSSION.

DR. W. H. WELCH: Dr. Smith's admirable contribution is an illustration of the unity of comparative and human medicine, and that, as Virchow long ago has said, the diseases of animals and those of man are of equal scientific interest, the only difference being in the dignity of the subject of the disease.

Dr. Smith has not solicited discussion on the etiology of Texas fever, but those familiar with the subject know that his discovery of a protozoöid parasite in the red blood-corpuscles of the subjects of this disease, analogous to the malarial parasite, is of the highest importance.

His description of the changes in the red blood-corpuscles in the anæmia of Texas cattle fever is of especial interest, inasmuch as similar changes are observed in certain forms of anæmia in human beings, particularly in profound anæmias resulting from loss of blood.

Dr. Smith's belief that the changes which he describes are all phases in one process is possibly open to question. It is, at least, well to consider whether there may not be other possible interpretations. Of the forms which he has depicted on the plate, I have been in the habit of regarding at least three as representing distinct forms, and not as transitional one to the other. The form with diffuse staining of the body of the corpuscle, described first by Ehrlich, is doubtless a developing, and not a degenerated, corpuscle. The form with a small number of deeply-staining particles of variable size I have hitherto interpreted as a corpuscle containing nuclear fragments. The small, regular granulations, staining with methylene-blue and more or less completely filling the body of the corpuscle, I have regarded as specific granulations in Altmann's sense, and not as transitional between the first and second forms mentioned. Dr. Smith's view that these three forms are transitional one to the other is interesting, and it may be that he has found in the blood of cattle affected with Texas fever an object of study which will afford a definite solution of this and some other unsettled questions in the physiology and pathology of the blood.

DR. PEPPER: Will Dr. Smith state the changes which he finds in the corpuscles in anæmia produced by venesection?

DR. SMITH: We get the whole series as shown, excepting the parasite. The impression which I have had from examination of from sixty to seventy cases is that we have a series of transition forms.

GRAVE FORMS OF PURPURA HÆMORRHAGICA.

By J. H. MUSSER, M.D.,
ASSISTANT PROFESSOR OF CLINICAL MEDICINE, UNIVERSITY OF PENNSYLVANIA.

As yet, we must assume for a classification of purpura the two forms of idiopathic and symptomatic. To the former belong all varieties, differing only in degree, for which no adequate pathological explanation has as yet been made. Hence simple purpura, purpura rheumatica, and morbus maculosis Werlhofii or peliosis rheumatica are of close kinship. While to the second of the above varieties belong those cases of hemorrhage due to the anæmias, to scurvy, to hæmophilia, to septic processes frequently; to some cachexia, as notably in carcinoma of the stomach; to the latter stages of hepatic disease and of Bright's disease, and to the curious forms of subcutaneous hemorrhage that arise in certain cases of sarcoma, particularly of the skin and bones.

In the present state of our knowledge such classification must stand, notwithstanding the able and exhaustive attempt of Wilhelm Koch[1] to give to all forms of purpura a common origin. In a most elaborate monograph on blood diseases, Koch treats of scurvy and the idiopathic purpuras. He does not see any adequate reason for regarding the purpuras as distinct from each other, or even from scurvy. He holds that purpura and scurvy are identical processes; both occur sporadically and epidemically; both have the same etiology; both have like symptoms; there is an affection of the gums in both, and there are hemorrhages in both. He regards scurvy as an infectious disease, characterized by disturbances of nutrition and caused by bacteria. The particular microörganism has not been determined satisfactorily as yet. His own experiments have been negative, but

[1] Wilhelm Koch: "Die Bluterkrankheit in ihren Varienten," Deutsche Chirurgie, Lieferung 12, 1889.

he believes the bacteria produce a toxine and are the cause of the nutritional disturbances.

Watson Cheyne, quoted in Fagge's *Practice*, found micrococci in the blood of a purpuric patient, and Klebs, Wickham Legge, Hlava, and others, found them in the purpuric patches. (See *Annual of Medical Sciences*, 1889.) Guiman also found microörganisms; but inoculated rabbits with pure cultures and produced purpuric eruptions. (*Annual*, 1889.) Litzerich, of Wiesbaden, suffered from purpura, and has been a voluminous writer on this subject; and recently (*Zeitschrift für klin. Medicin*, Bd. lxxx., Heft 5 u. 6, 1891) makes further report of his own and other cases. With Koch's culture method he has been able to demonstrate the bacillus. It resembles the bacillus of anthrax, but differs in size and form. The spores of the anthrax are smaller and rounded. They differ slightly when growing on culture medium. The bacillus of purpura forms no toxine as the anthrax bacillus does, but a weakly acting ptomaine; hence, there is little fever in purpura. Further studies of the spores were made.

The present notes are simply a record of some grave forms of idiopathic purpura, and in their detail it will be found that the gravity of the different degrees are dependent either upon an excess of hemorrhage into internal cavities, or to the exterior, and death on account thereof, or upon an excess of hemorrhage plus the occurrence of a process certainly septic in its characteristics, such sepsis having occurred either primarily or secondarily to the subcutaneous and submucous hemorrhages. Indeed it is in the grave forms of purpura that one readily sees the symptoms of an infectious process. Thus, hemorrhages subcutaneous and submucous arise, extensive œdema develops, inflammations of cutaneous, mucous, and serous surfaces take place, attended by fever and all the phenomena of septicæmia. The writer holds, however, that in the present state of knowledge the febrile process is entirely secondary, and that in its true autonomy purpura does not present any septic symptoms. The first and second cases reported illustrate grave forms due to excessive hemorrhage; the third and fourth cases are examples of extensive hemorrhages, sloughings, internal inflammations, and secondary fever, apparently of septic origin. The fifth case had most interesting associate phenomena. It appeared to be a case of purpura of rheumatic origin, the hemorrhages being replaced by another rare manifestation of

rheumatism—hyperpyrexia. Not only are the cases interesting as the story of an obscure yet well-defined process in the economy, but also because each presents individual difficulties of diagnosis. With the history of each case the problems that arose for solution will be discussed.

CASE I.[1] *Hæmatemesis of considerable duration, originating in the œsophagus; fibroid tumor of the uterus; general purpura; death from retro-peritoneal and mucous hemorrhages.*—The patient was a female, forty-eight years old. She had always been well, except the past three years, during which time, as the menopause approached, the hemorrhages of a large fibroid caused much loss of strength. She lived in the country, was always well-to-do, never worked hard, and had good food with much variety. She never had cause for anxiety. She never bore children. She never had rheumatism. There was no history of "bleeders" in the family, and otherwise the family history was good.

A few weeks before the writer saw her with her attending physician, Dr. Bartleson, she began to vomit blood. The discharge of blood was preceded by pain behind the xiphoid cartilage, with oppression. The blood discharged was bright in color, not frothy, lightly coagulated, and rarely mixed with stomach contents. It was discharged irregularly—once or twice daily, or every second day. Food did not excite the hemorrhage. Vomiting did not take place, except when blood was discharged. All functions of the body were normal, and all the organs apparently free from disease, except the uterus, in which a large fibroid could readily be detected by abdominal palpation.

In spite of treatment, the hemorrhages persisted at irregular intervals. Two months after the writer saw her, purpuric spots developed on the legs, and rapidly extended over the rest of the body, while conjointly hemorrhages from the mucous membranes took place. Ten days after the subcutaneous hemorrhages arose she died in syncope, with symptoms of an internal hemorrhage. At the autopsy hemorrhages from all the mucous membranes were found, particularly in the gastro-intestinal tracts and the respiratory and genito-urinary systems. A large retro-peritoneal hemorrhage was the cause of death. The space behind the peritoneum from the diaphragm into the pelvis was packed with clotted blood. The œsophagus appeared dilated and the œsophageal veins enlarged. A small pin-point hole through the mucous membranes into a vein was the seat of the early œsophageal hemorrhage. A small clot covered the surface, but the veins were not the seat of thrombi. The fibroid tumor previously mentioned was as large as a child's head.

REMARKS.—Early in the case the source and cause of the hemorrhage were obscure. The writer believed it to be of œsophageal origin,

[1] See Transactions Phila. Co. Med. Soc., 1887.

because of its character, because it was not mixed with food, and because a source for it could not be found in the pharynx. It was not gastric, because repeated stomach-washings failed to show the presence of any blood in the gastric contents on microscopical examination. The writer further thought that it was due to a varicosity of the veins around the end of the œsophagus, which might be dilated because of an obscure cirrhosis of the liver. Again, such dilation might have arisen on account of thrombi of intra-abdominal veins, due to the presence and pressure of the uterine fibroid. Apart from a mechanical explanation of such nature, no clue could be devised. The occurrence of the general purpuric symptoms cleared up the case.

CASE II. *Purpura rheumatica; vomiting; two relapses; tenderness of the abdomen; hemorrhages from the bowels.*—R., aged fourteen; school-boy; West Philadelphia. Seen in consultation with Dr. Birney. Patient was always well; he never had rheumatism; the parents are not rheumatic, and the family history is good.

On the evening of November 19, 1890, a few purpuric spots were noticed on the leg.

On the 20th there was swelling of both ankles and pain on movement, which, with the purpura, kept the patient in the house.

On the 21st the arms were covered with spots of purpura and the elbow-joints were swollen and painful, with diffused, dusky hue of the skin. The right joint improved during the day, the left joint remained bad.

22*d*. Boy vomited some blood this morning and stomach remained irritable all day; associated with pain in the abdomen. When visited by the writer at 5 P.M., the boy was then, and had been, suffering from very severe nausea, with occasional vomiting of watery fluid. Blood was seen in the matter vomited, and early in the morning it was said that the blood was coagulated. The patient was pale and looked prostrated, surface cold, and on taking temperature the thermometer was kept in the mouth twelve minutes before it rose to 98°. Over feet and legs bright-red purpuric spots were seen; some of which were much darker, faded since morning. On arms more recent purpuric spots, irregular in shape, from split pea to the size of a three-cent piece, with dark centres and red periphery, the centre usually about one-third the size of the entire spot. Many of the spots were elevated and some few were tender—this was particularly so of a couple of old spots on the toes. The color of them did not disappear on pressure at all. The left elbow-joint was the seat of a diffuse swelling, with tenderness on movement. The swelling seemed to be entirely outside of the joint. The pulse was from 124 to 130; heart normal. Bowels had not been moved in twenty-four hours, and an examination of the abdomen showed it to be distended and very

tender all over; the point of greatest tenderness was in the left iliac fossa about the sigmoid flexure. There was no tympany. The tongue was heavily furred. On examination of the throat the right tonsil was seen to be enlarged and dark-red in color, and the post-pharyngeal mucous membrane was quite injected. No hemorrhages took place from the mucous membranes. The urine was clear but very acid, and was said to contain phosphates but no albumin.

Blood-count. Red corpuscles 5,500,000. White not increased. Hæmoglobin 75 per cent.

One week after first note the patient had second eruption. Dr. Birney writes: It was very extensive over the legs and arms, and was ushered in by profuse vomiting and gastric pain, and profound weakness followed. Pulse 120. Five days after he again picked up strength and appetite, both of which he had had prior to the development of the second eruption. During the relapse blood was passed from the bowels. Four or five movements each day contained one to two ounces of blood, dark in color.

Dec. 14. (Further notes by Dr. Birney.) No return of hemorrhage from the bowels; since last note passages loose but natural. Patient now in the midst of attack of vomiting, which has lasted eight hours, and during the latter part of it small purpuric spots appeared. The vomiting was associated with gastric pain; the matter vomited was dark-red fluid, resembling beef-tea, with shreds in it; discoloration probably due to blood. Creasote checked it at third attack. Boy suffers considerable with rheumatic pain at the joints, particularly at the elbows; these pains are always worse with the new crop of eruption, and are relieved by painting the parts with salol and collodion. The septum of his nose is almost entirely ulcerated away, leaving a large perforation in the cartilaginous portion. He is extremely emaciated, but getting along pretty well. No trouble with the urine. Tongue clean now, but bright. One large purpuric spot had appeared in the middle of the tongue; it lasted five days, leaving no trace after its absorption. Appetite varies and is capricious.

Patient entirely recovered after a most tedious convalescence.

REMARKS.—The diagnosis was easy. The gravity of the disease is not brought out sufficiently by the history. The prostration was sufficient to render the liability of death to ensue at any moment. The extreme tenderness of the abdomen was remarked. It was possibly due to subperitoneal hemorrhage.

The writer described elsewhere the death of a child, aged nine months, from purpura. The child was of healthy parentage, fairly well nourished by the mother. Internal and external hemorrhages caused death. The blood oozed through the skin, particularly on the cheeks, clotting as it appeared on the surface.

CASE III. *Purpura rheumatica in a patient with old valve lesion; pericarditis; gangrenous slough of the uvula, simulating diphtheria; recovery.*—S. C., aged twenty-six years; male; mechanic; well nourished and of good habits. He had rheumatism in early life. Otherwise he was always well and was not of a family of bleeders.

Four weeks before the writer saw him with Dr. Longenecker, the patient had a sore throat. On May 11th he had a slight attack of rheumatism of the joints. May 15th sore-throat again. May 16th, purpura and at the same time paralysis of the fauces. The food regurgitated through the nostrils. On May 20th seen by the writer. Hemorrhage beneath skin of arms and legs. Vibices on the back. Œdema of the eyelids; conjunctival hemorrhage. The subcutaneous hemorrhages are round, elevated, tender on pressure, and of variegated color, depending on their age. In many a peripheral zone of hemorrhage encloses a pale area, in the centre of which in some a hemorrhagic spot is seen. They cover the extremities and trunk.

Temperature 103°; pulse 120. Severe præcordial pain. Pericardial friction-sound; loud mitral and aortic murmur, systolic in time. Apex of heart in sixth interspace; impulse diffused, area of dulness increased. Uvula swollen, dark-gray color on surface, with pellicle not unlike diphtheria; fauces congested. Joints swollen and painful. No sweats. Urine does not contain albumin.

21*st*. Temperature 102½°; pulse 110; muscle and joint pain; pericardial friction less. Uvula sloughing at the base. Vomiting.

22*d*. Uvula sloughed off and swallowed. Temperature 102°; pulse 110. Joints not relieved. Subcutaneous hemorrhage fading.

23*d*. Temperature 100°. Patient anæmic; murmurs in vessels and at base of heart and tricuspid.

No further history need be detailed except that recovery took place after a long and tedious convalescence.

REMARKS.—The patient evidently had diphtheria originally in a mild form. Simultaneously with the development of the post-diphtheritic paralysis, the purpura developed with the joint complication. The sloughing uvula suggested a second attack (?) of diphtheria. The cardiac lesion added to the possibilities of the case. The enlarged, dilated heart indicated that the valve lesions were not recent.

It is scarcely worth while to discuss the differential diagnosis of the various possible processes. A bacteriological examination of the uvula shreds would have excluded diphtheria, as was done because the appearances were not sufficiently characteristic, the affection was so localized, the glands were not enlarged, the general symptoms were proportionately greater than the local.

Was it a case of malignant or rheumatic endocarditis? Cardiac

murmurs, fever, sweats, joint symptoms, subcutaneous hemorrhages, many of which looked like hemorrhagic infarcts, pointed to endocarditis. No hemorrhagic infarcts were present in the mucous membranes; the spleen was not enlarged; the urine was normal; the murmurs were due to old valve lesions.

The above was written after the writer attended the case, three years ago. In the light of the subsequent case, the difficulty of deglutition appears to have been due to the swollen, unyielding uvula. And, therefore, probably the patient did not have diphtheria when he had his first attack of sore-throat.

CASE IV. *Relapsing purpura, with joint symptoms, great œdema, sloughing of the skin, sloughing of the uvula; hemorrhages from mucous surfaces; marked reduction in hæmoglobin; no reduction in number of red corpuscles.*—W., aged twenty-four, German, but recently a resident in Philadelphia, cutter in tailor establishment, visited me at my office on the 13th of April apparently suffering from an ordinary severe cold. He had an acute catarrh of the nose, œdematous pharyngitis and slight bronchitis with it, and he suffered from headache and general pains. He was not feverish, and, except from the discomfort of occluded nostrils and cough, did not appear to be very ill. He attributed this cold to exposure from bicycle riding, but stated that during the previous week he had three chills at intervals of two days, one of which was so severe and attended by such high fever and general aching with head pain, that he left his work for the afternoon. This occurred on the 9th of April, on which he also had four attacks of nose bleeding. Two days after his visit, or on the 15th of April, I found him in bed with rather diffused purpura accompanied by rheumatic pains. The forearm became swollen, tender, and painful, and large subcutaneous hemorrhages at both elbows were seen. The hands were attacked at the same time. The pains were described as of a burning and smarting character. The thighs and arms were very stiff. The eruption on the first day was confined to the legs and was composed of large maculæ, some with central darkening, others with peripheral. No headache and but little fever; urine normal; bowels constipated; stools at times yellow, at times black. In three days the eruption (which will be described later on) almost entirely disappeared and the patient felt free from pain, so that by the 21st he was quite able to sit up.

On the 22d a severe attack of dry pleurisy of the left side came on, which was relieved by a blister. On the 23d a relapse took place. In addition to the purpuric symptoms, sore-throat and spitting of blood were observed, and on swallowing food came out of the nostrils. 25th, grayish pellicle on swollen uvula. The joint symptoms on the 27th became more severe, and there was a recurrence of the eruption in its most aggravated form.

On the 27th there was also œdema of the eyelids and swelling about the knees. On the 28th the very severe eruption was most abundant, and œdema

of the eyelids was quite extensive; several hemorrhages into the mucous membranes of the conjunctiva were seen. In the afternoon severe sore-throat developed, and on inspection there was intense redness of the fauces with extreme swelling and œdema of the uvula and soft palate. It was of a dark-red hue.

On the 29th the intense congestion and œdema led to sloughing of the uvula, the necrosis beginning on the right side and extending around the tip. This continued with some odor and but slight pain in swallowing until the 31st. Occasionally the patient would cough and there would be expectoration of blood or blood-stained mucus. This cough was most exasperating. Prior to the pleurisy there were present râles in the larger bronchial tubes, although faucial inflammation may have caused the cough then. Apparently œdema of the mucous membrane of the bronchi caused the cough. The œdema of the eyelids was most marked by the 29th and was not confined to the upper, but included also the lower lid. One eye was entirely closed, while chemosis was marked. There did not appear to be any inflammation of joints, but rather subcutaneous œdema with tenderness about the joints. The outline of the elbow-joint was changed entirely and the œdema extended down the forearm to the wrist, particularly on the right side. The knee-joint, the leg, and the ankle were swollen and painful.

With the relapse of the 27th the eruption recurred in its severest form, although possibly not with such large hemorrhages; petechiæ were abundant, but no vibices. Several crops took place from this time until May 6th, particularly recurring with peculiarly varied characters which will be hereafter described. With the return of this rash there was also œdema, but not so extensive. Latterly the large joints and forearm of the left side were affected more than the right, although the right eyelid was the most œdematous. The genital organs became very œdematous and the urine had to be drawn. There was phimosis. There was noted an abrasion, or rather superficial ulceration, but no pustulation on the scrotum. The subcutaneous hemorrhages of the scrotum became most intense by May 1st, and a slough formed and lines of demarcation were distinct by the 5th of May. The tissues to the depth of an eighth of an inch were lost, and the slough was about four inches square, irregular in outline.

Blood examination. April 29, 1890. Red blood-corpuscles, 4,660,000. Hæmoglobin 34 per cent.

30*th.* Hæmoglobin 30 per cent.

May 1. Hæmoglobin 27 per cent.

3*d.* Hæmoglobin 37–38 per cent.

22*d.* Red-blood corpuscles, 4,670,000. White, 80,000. Hæmoglobin 46 per cent.

Description of eruption. The appearance varied. Some were like the typical pupuric eruption.

April 23. Petechiæ on back painful, varying in size from a pea to a ten-cent piece. In many the centre was deep red, in others the periphery was more red and apparently the seat of the hemorrhage, having the form of the wheal of an urticaria. Some were perfecty regular in outline, others irregu-

lar. Again the centre of some would be dark red, then there would be an intermediate pale zone, and then a red zone in the periphery. Often many were somewhat irregular in outline. Still again, others of the petechiæ would be uniformly red with regular uniform outline. In others the outline was marked and then a dark centre arose from an elevated white base. The centre was made up of innumerable punctate hemorrhages. Some spots were as large as a half dollar.

May 2. New bright red, large, irregular petechiæ and small, round, elevated ones with capillary hemorrhages in the pale central zone, near the periphery.

Further notes. Eye-ground examined by Dr. de Schweinitz, May 28th; nothing abnormal. Marked pallor of face. It may be said that the urine was normal; not bloody at any time. No hemorrhages from other mucous membranes took place. No nervous symptoms, no tenderness in the course of nerve trunks, but some tenderness in the spine from fourth to seventh dorsal vertebræ. Pulse not increased in frequency, and there was no fever except when the sloughing was at its height. No gastro-intestinal symptoms of note. Bowels constipated, no change in color.[1]

REMARKS.—I am not aware of any observation regarding the reduction of hæmoglobin. In this case it was remarkable and was greatest when the disease was at its height. The case was one of peliosis rheumatica, as described by Schönlein. It was not difficult to recognize.

CASE V. *Malignant purpura; gastro-intestinal and subcutaneous hemorrhage; joint symptoms; hyperpyrexia; death on the sixth day; no autopsy.*—As an example of a malignant form of purpura, let me refer for a moment to the following case which occurred in the practice of a medical friend who asked me to see it with him in consultation. The patient was a young lady, twenty-three years of age, single, a resident of Harrisburg, Pa. She came to this city on a visit, and was taken suddenly ill with extreme nausea, which lasted an hour, followed by vomiting, at first of a slightly acid fluid and afterward of large amounts of blood. The vomiting was followed by diarrhœa attended by severe colicky pains. The stools were loose and watery, and finally dark and tarry. This was on the 25th of March; next day, the 26th, a general purpura was seen limited to the extremities, extending over the legs and thighs, and the hands and forearms; with the development of the rash, the gastro-intestinal symptoms lessened, and by Tuesday morning (27th) they had ceased entirely. On Monday, however, the joints were noted to be very painful on motion and pressure, and much swollen.

The writer saw her on the 27th with a temperature in the evening of $102\frac{2}{5}°$

[1] A friend made inoculations of blood secured from the patient on various culture media and likewise on rabbits and guinea-pigs. As mentioned by Dr. Welch in the discussion, the only bacteria secured were from the skin.

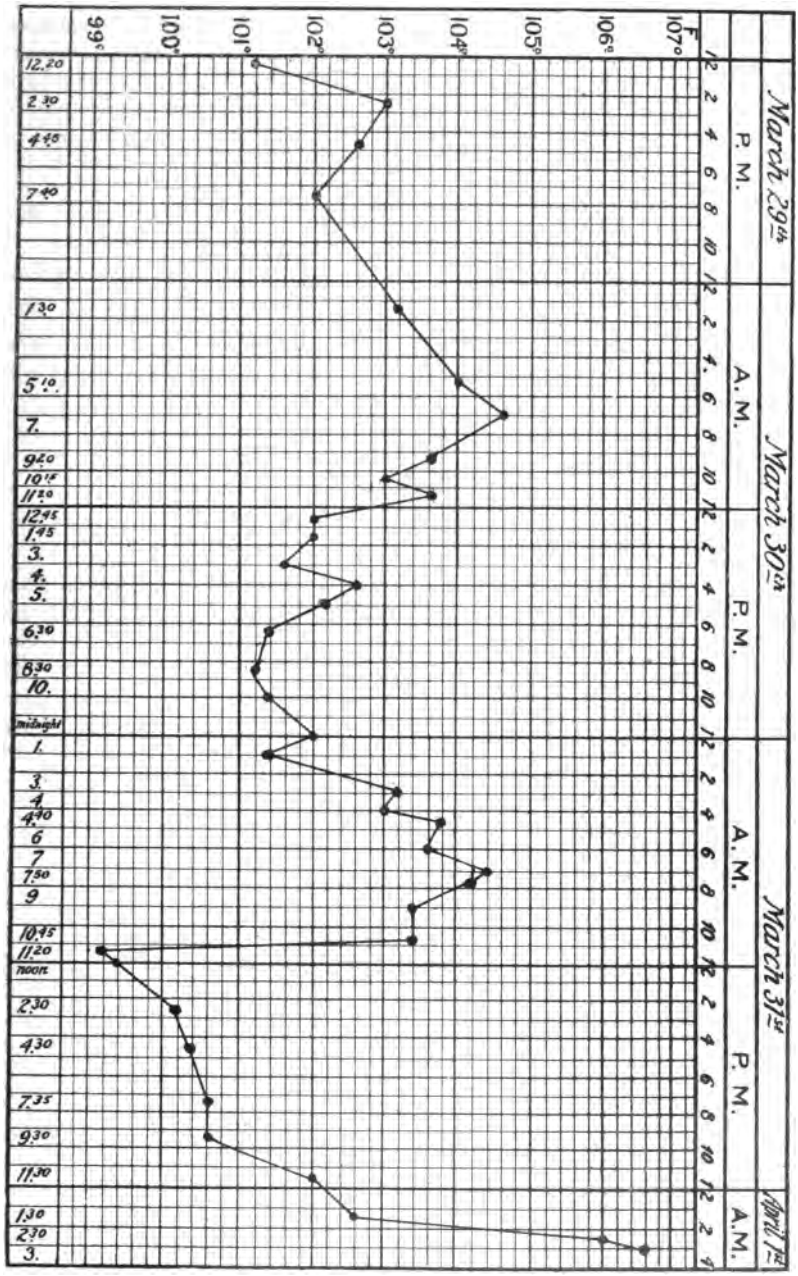
pulse of 110, respirations 24. She was decidedly hysterical; the gastro-intestinal symptoms were in abeyance; the purpura was marked, as were also the joint complications. She suffered from excruciating headache, and at the time of the visit this was the most marked symptom. It was constant, but paroxysms of extreme severity took place. There were no evidences of brain lesion, no strabismus, and no paralyses, local or general, no twitchings, no change in the sensation. The urine had been examined and was found to be normal. We visited her together daily until her death, which took place on the 31st. Several features of interest occurred during this time, each of which will be detailed from the daily notes.

On the 28th, in the morning, the temperature was 104°, the pulse 120, the respirations 25. In the evening the temperature was 102°, and the respirations and pulse about the same. The purpura and the rheumatic symptoms continued, as did also the severe headache. She had no movement of the bowels. It was thought either that the case was one of rheumatic purpura with associate hyperpyrexia, or the possibility of an obscure form of malarial fever was considered at the suggestion of Dr. Dunot, who had been her family physician, and who saw her in consultation. The blood was examined in order to determine the presence or absence of malaria. It was found to be fairly healthy, and formed rouleaux normally. The proportion of the white corpuscles was normal, except that there was a slight increase of the small lymphoid forms. There were no plasmodium or any foreign elements, except a few pigment granules which were found in one white corpuscle. The blood plaques were not increased, and the color of the red corpuscles not notably altered. The spleen was not enlarged. There was no evidence of organic disease anywhere present.

On the 29th, the temperature was 101⅕° in the morning, 103° in the afternoon. She had two movements of the bowels, slightly formed. The pain in her head had improved somewhat, and her mind was perfectly clear. She was not so hysterical as she had been. The joint symptoms were relieved by the use of the salicylate of soda, both by the stomach and rectum. Violent conjunctivitis and iritis set in to-day. Both were believed to be of rheumatic origin.

On the 30th, at seven in the morning the temperature was 104⅘°, in the evening at five it was 102⅕°. The pulse at both times was 130. The headache was much more severe and continuous than it had previously been, the purpura remained the same, and there were no other symptoms.

The night of the 31st she became delirious, although no typhoid symptoms had developed. The temperature at seven o'clock in the morning of the 31st was 104⅘°, while during the night it ranged from 102° to this point. It had been taken hourly. The delirium gave way to stupor at this time. On account of the high temperature cold pack was used, so that by eleven o'clock of the 31st the temperature had fallen to 99⅕°. In spite of the internal administration of antipyretics, it continued to rise from this time, so that at twelve o'clock it was 102°, when on the morning of the 1st of April it rose to


March 29th
March 30th
March 31st
April 1st
P. M.
A. M.
P. M.
A. M.
P. M.
A. M.
99°
100°
101°
102°
103°
104°
105°
106°
107°
F.
12.20
2.30
4.45
7.40
1.30
5.10
7.
9.20
10.15
11.20
12.45
1.45
3.
4.
5.
6.30
8.30
10.
midnight
1.
3.
4.
4.40
6.
7.
7.50
9.
10.45
11.20
noon.
2.30
4.30
7.35
9.30
11.30
1.30
2.30
3.

106½°. The stupor of the 31st rapidly gave way to coma which continued until her death, which took place eight hours after the coma developed. During the night she had a profuse nosebleed, and there was considerable expectoration of blood, which appeared to be from the bronchi. The high temperature, the continuance of the purpura, the grave cerebral symptoms alone marked the course of the disease during the last forty-eight hours of her life.

Unfortunately an autopsy was not allowed, but it is possible she might have had a cerebral hemorrhage, and yet scarcely probable.

I take it to be one of those cases of purpura hæmorrhagica which appear to be on the borderland, and which we cannot separate distinctly from rheumatism, or, on the other hand, call it a true purpura. I believe that the purpura, the joint symptoms, and the hyperpyrexia were all rheumatic.

DISCUSSION.

DR. WELCH: A word about the micrococcus found by Dr. Musser. This coccus was probably the white staphylococcus which is found regularly in the epidermis, at least there is nothing in Dr. Musser's description of the characters of the coccus in opposition to this view. The procedure employed would not have thoroughly disinfected the skin, and, moreover, the staphylococcus albus exists not only in the superficial but also in the deeper layers of the epidermis. Dr. Musser very properly attaches no especial importance to the detection of this organism.

DR. PEPPER: I saw during the last year two grave cases of purpura in school-children of about eleven and thirteen years. There were in both cases extensive hemorrhages with subsequent suffering. Curiously enough, in both cases complete destruction of vision in one eye occurred from filling of the globe of the eye with blood. I may add, that after the subsidence of the epidemic of influenza in Philadelphia there appeared to be an unusual tendency to purpuric affections. I will mention but two cases in which I suspected the peculiar eruption to be associated with an influence of this kind. Both were cases of rötheln, occurring in the same house. The first patient was a lady of about twenty-eight. The symptoms were typical and the eruption highly characteristic. On the second day there came sudden hyperpyrexia, temperature 105°, and with this all the spots of eruption became petechial, and there were some larger subcutaneous hemorrhages. There was no other appearance of gravity in the case. There were no nervous phenomena. The fever subsided rapidly at the close of the third day; convalescence was immediate and complete. The petechia were rapidly absorbed.

The second case was the attendant upon this lady, who developed rötheln

in eight days after the initial symptoms in the first case, and who passed through an attack identical in its features with the above, including hyperpyrexia, and the eruption rapidly became petechial.

DR. D. W. PRENTISS: I had the honor to present a case of purpura hæmorrhagica to the Association at its last meeting. It was an exceptionally grave case, and was marked by periodic exacerbations. He was sick for a little over a year. It commenced with very violent symptoms of purpura, with joint affections, and with intense suffering. He would recover from an attack in ten days to three weeks, and then in about six weeks these symptoms would recur with very great violence. The two most characteristic symptoms in his case were the hemorrhages in the different portions of the body—from the bowels, from the bladder, but never from the lungs—and hemorrhage under the skin. A peculiar feature of this case was sloughing of the skin from two of these hemorrhages which occurred in the abdomen. Within the space of half an hour the hemorrhage occurred in the skin of the abdomen on each side of the umbilicus, about the size of the palm of my hand, and turned intensely black; gangrene developed, it separated just as any other gangrene would, and it healed by granulation. He has the scars yet.

Another instance of sloughing was in the prepuce. The patient had a very tight phimosis, and a slough occurred in the prepuce which cured the phimosis and cheated the surgeon out of an operation. A very marked class of symptoms in his case was that simulating peritonitis and enteritis. It was these symptoms that threatened life, and it seemed to me that at each recurring attack he must die. I brought him before the Association in the interval between the relapses in order to show these scars which the slough had produced, as I had not found, in my reading, that mentioned as one of the symptoms of purpura. In the discussion of the case, it was suggested by two members that the best treatment of the case would be by phosphorus. I had found arsenic, up to that time, to do the most good; but it did not prevent relapses. I put him on phosphorus and he began to improve; the relapses occurred with lengthening intervals until they stopped altogether, and the boy entirely recovered. I believe his recovery is due to phosphorus, and that the boy owes his life to this Association.

DR. GRAHAM, of Toronto: Dr. Jacobi and I were the two that suggested phosphorus. I use it in the form of phosphide of zinc. The only fatal case of purpura hæmorrhagica I have ever had under my observation was one in which death took place as the result of an enormous clot that formed in the bladder, distending it so that the fundus reached the umbilicus. In that case the phosphorus had not been used.

DR. PEPPER: Is it a fact that in these cases of purpura the blood does not exhibit the same changes as in anæmic cases?

DR. THEOBALD SMITH: Dr. Prentiss asked me to examine the blood of his case. I found only the uniformly tinted cells referred to in my paper.

BRADYCARDIA (BRADYSPHYGMIE–OZANAM) IN ACUTE RHEUMATISM.

By I. E. ATKINSON, M.D.,
PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS AND OF CLINICAL MEDICINE IN THE UNIVERSITY OF MARYLAND.

Bradycardia, or abnormal infrequency of the pulsations of the heart, is present, according to recent writers, whenever the heart-beats number less than sixty to the minute. It is undoubtedly a very rare symptom during the course of acute articular rheumatism, and nearly all writers upon this disorder do not refer to it.

It is not a little surprising to learn that a not insignificant proportion of hospital patients, studied with reference to the frequency of the heart-beat, should have presented this phenomenon. Of 3578 patients treated at the Zurich clinic[1] during the years 1884–86, 82 or 2.29 per cent. had bradycardia, and of 7567 cases treated at the Giessen clinic[2] during seven years this symptom was present in 1041. At the Zurich clinic during the years indicated, 286 cases of articular rheumatism were treated, and of these 24, or 8.39 per cent., had bradycardia. Riegel tabulated 42 cases of bradycardia from a total of 144 cases of articular rheumatism treated at the Giessen clinic. This author, however, considered the symptom as occurring during convalescence from acute articular rheumatism and not during its active stage, and attributed it not to any specific rheumatic influence exerted upon the heart, but rather to the heart exhaustion which, according to Traube's theory, is the cause of slow action of this viscus during convalescence from various acute febrile diseases. Were this true of all cases, bradycardia arising after rheumatic fever would

[1] Grob: Arch. f. klin. Med., Bd. xlii., 1888, p. 574.
[2] Riegel· Zeitschr. f. klin. Med., Bd. xvii. p. 228.

not especially interest us; but while, in fact, it does occur in most cases after defervescence and during convalescence, it assuredly does not so occur in all. Even Riegel's own cases, a portion of which served Bötticher[1] as a basis for his own essay upon bradycardia, afford reasonable evidence that such an explanation cannot be universally applied. Bötticher reported 26 cases of articular rheumatism in 294 cases of bradycardia. At the time of the appearance of the bradycardia nearly all patients were without fever, but in some cases fever was present even when the pulse was clearly slowed.

Admitting, then, that it is usually during convalescence from, and not in the course of rheumatic fever that bradycardia has been encountered and that, when thus occurring, it usually has its origin in a cause common to convalescence from a number of acute febrile disorders, we cannot accept such explanation for cases occurring at the outset or during the height of the rheumatic seizure. That bradycardia does occur under such conditions is certain, though, it must be confessed, recorded observations are exceedingly few. It has been encountered both where rheumatic cardiac complications were concurrently detected and where such changes could not be recognized. Of the 26 cases reported by Bötticher, manifest cardiac alterations were present in only 9; but of the 17 cases in which such changes were not detected, it was not stated how many were already convalescent. Grob's report is more definite, though he has not attempted to draw sharp lines. 11 cases, in which bradycardia was developed after the subsidence of or in the absence of fever, showed no cardiac symptoms whatever; but of 13 cases in which cardiac inflammation was present, 6 developed bradycardia during the persistence of fever.

It is not the object of this paper to discuss bradycardia simply as an epiphenomenon of convalescence, though, in passing, it may be said that the widely accepted theory of Traube, regarding the causation of this symptom after acute febrile disorders, that of "heart-tire," can in no measure be applied to many of those cases occurring after rheumatism in which fever and increased heart-action have been altogether insignificant. The much rarer phenomenon of bradycardia during the course of, and not after, acute rheumatism will be more especially considered, first in its clinical and then in its etiological relations.

[1] Inaug. Dissert., Giessen, 1888.

It has been my fortune to treat two cases of acute rheumatic fever in the course of which bradycardia was developed. These and several other cases found in medical literature form the basis of my remarks.

CASE I.—D. B., a colored youth, nineteen years old, well built and muscular, previously healthy, and without family or personal history of rheumatism; took a cold bath on the night of April 5th, and early next day rode twenty-eight miles on a bicycle. Since then he had not felt well. He was sore, and had pains through his chest and legs. I saw him on the 12th. He then had pains in the thighs, His knee-joints were swollen and tender. Pulse 92, temp. 102.5°. His tongue was coated with a white fur, and his skin was bathed in sweat. There was præcordial pain. A slight "to and fro" friction-sound could be heard along the left sternal border. He was ordered to take twenty grains of sodium salicylate every two hours. The affected joints were wrapped in cotton.

13*th*. Temp. 100°, pulse 90. There was no joint pain, but there was marked præcordial distress. The pericardial friction was still present.

14*th*. The joints were fairly free. There were severe chest pains. The breathing was hurried, and there was some agitation of manner (effect of salicylate?). Every fourth hour to have one-eighth grain of morphine sulphate.

15*th*. Profuse and persistent epistaxis. Temp. 101.3°, pulse 90, resp. 30. No joint pain. The salicylate was discontinued on account of its unpleasant effects.

16*th*. Again very profuse and exhausting epistaxis. Temp. 100°, pulse 90. Much prostration. With a view to check the epistaxis, and to prevent its recurrence, a fluidrachm of the following mixture was given every fourth hour:

℞.—Fluid ext. digitalis . . . . ♏ xxiv.
Fluid ext. ergot . . . . . f ʒijss.
Fluid ext. ipecac . . . . . ♏ viij.
Aquæ . . . . . ad f ʒii.

The area of cardiac dulness was not increased. The friction-murmur persisted along the left sternal border. In the nipple line and slightly beyond a remarkable cardio-pleural friction sound could be heard. It was notably modified by the respiratory movements. It was close to the ear, and distinctly rasping and dry. At the beginning of inspiration it was heard during systole and diastole, but at the height of inspiration it quite disappeared and only the soft substernal friction could be heard; as expiration was completed, it reappeared. If the patient held his breath either in inspiration or expiration it was no longer heard. The sound was evidently produced by the action of the heart, but depended upon the coöperation of the respiratory organs, and was apparently due to a circumscribed pleuritis. It never extended, and no other signs of pleuritis developed. There was still præcordial pain.

17*th*. Tongue coated. Temp. 98.3°, pulse 45 at 11.45 A.M. He had had no

digitalis since 11 o'clock the preceding night, and was now only taking one-eighth grain of morphine sulphate every fourth hour.

18*th*. Temp. 97°, pulse 54. No epistaxis. Pericardial friction-sound (not influenced by respiratory movement) was heard most distinctly in the third intercostal space at the left sternal border. It was double, resembling the crumpling of parchment. He was now given thirty grains of potassium citrate every fourth hour.

19*th*. Pulse 54, temp. 97.5°. A soft systolic murmur could be heard both at base and apex.

20*th*. Temp. 99.2°, pulse 60, with some dicrotism. A small blister was applied to the præcordial region.

21*st*. Pulse 64, resp. 18, temp. 99.4°. Pain in the right shoulder and knee, which were swollen and tender.

23*d*. Pulse 64, resp. 18, temp. 100.4°. Return of acute rheumatic symptoms. Sodium salicylate in twenty-grain doses every second hour. No friction sound. A soft and prolonged basic systolic murmur. Slight epistaxis.

24*th*. Pulse 60, temp. 100.2.° Less pain. No pleuritic friction.

25*th*. Pulse 59, temp. 99.2°. Reappearance of the friction-sound all over the cardiac area, but most intense toward the sternal border. More comfortable. No pain in the chest. Cardiac dulness not increased. Sodium salicylate to be given every fourth hour.

26*th*. Temp. 98.4°, pulse 60. No joint pain. Friction heard along sternal border.

28*th*. Slight epistaxis. No joint pain. Temp. 98.4°, pulse 58. Pericardial friction and basic systolic murmur marked. Salicylate only three times daily.

29*th*. Temp. 98.4°, pulse 48. Friction very marked, superficial and crackling. No pain. Bowels always freely respond to mild stimulation.

May 1. No pain. Pulse 52, and slightly dicrotic. Friction indistinctly heard, and only along the left sternal border.

4*th*. Temp. 100°. Pain in the left shoulder and small of the back. Copious sour sweat. Salicylate resumed at intervals of two hours. Pulse 72.

6*th*. No fever. Pulse 72. No friction-sound, pericardial or pleural. Persistence of systolic basic murmur. Had taken no medicine for a number of days. Slight stiffness of joints, otherwise well.

CASE II.—M. Y., a student, twenty years old, of delicate frame; had acute rheumatism when eleven years old, and with it cardiac complications. He consulted me on account of intra-thoracic pains and palpitations, in October, 1889. He then had much hypertrophy of the left ventricle and a loud mitral systolic murmur. His pulse, at several observations, varied between 72 and 90. On the afternoon of March 12th, 1890, I was called to see him. He was in bed. His expresion was anxious; he was very pale and complained bitterly of pain in both elbows and knees. His temperature was 102°, and his pulse rapid, but not recorded; it was weak and exceedingly irregular. Tongue coated with thick white fur; bowels constipated; skin bathed in sweat. He was given a purge, and was ordered to take thirty grains of potassium citrate

four times daily, and for his feeble and irregular heart-action two drops of fluid extract of digitalis every fourth hour.

13*th*. Somewhat better, but has intense epigastric pain, angina-like in character, with a sensation as of impending dissolution. The pulse was still feeble and irregular and somewhat less frequent. The joints were easier.

14*th*. Pulse 60 and regular. Digitalis stopped. Epigastric pain still intense.

15*th*. Very pallid. Epigastric and præcordial pain agonizing. Pulse weak, extremely irregular, and beating from thirty-two to forty times per minute. An interval of six seconds was counted between two pulsations of the heart. The joint pains were much better. Morphine sulphate one-sixth of a grain hypodermatically every third hour.

16*th*. Joints much better. Temp. 99.5°, pulse feeble, irregular, 60, 65, 70. Epigastric and præcordial pain still most severe. Morphine continued as before. Sinapism to painful area. Potassium citrate grs. xl. every fourth hour.

17*th*. Pain still excruciating, only modified by morphine. Temp. 102°, pulse 56, irregular and small, not affected by change of position. Much pallor and anxiety of countenance. Free diaphoresis. To-day, for the first time, a pronounced "to-and-fro" pericardial friction-sound was superadded to the valvular murmur. The pains in the joints were less pronounced, but the præcordial pain was even more intense, a dart of pain being felt with every heart-beat. This pain was still alleviated but not removed by hypodermatic injections of morphine (one-fourth of a grain) every third hour. Tablets of nitro-glycerin ($\frac{1}{100}$ of a grain each) were now given every second hour. The effect of these was to cause flushing of the face and quickened, though still irregular pulse.

18*th*. Temp. 100.1°, pulse 108 and regular. Rests more easily under morphine. The pericardial friction was modified but widely diffused over præcordial region. Improvement now followed. Slight pericardial effusion appeared and underwent slow absorption. The fever and joint symptoms gradually subsided, and without recurrent bradycardia and under tonic treatment he was able to leave town for home in five weeks.

Somewhat resembling the foregoing case is the following one reported by Blachez.[1]

CASE III.—A man, aged fifty years, had had several attacks of rheumatism which had not involved the heart. When seen by Blachez he had severe rheumatic pains and a pulse-rate of 84 to 90. The heart-beats were strong and without murmur. Toward the eighth day of the malady, which had been treated with sulphate of quinine in doses of 0.80 to 1.20 grams daily, he was seized suddenly with alarming cerebral symptoms and during the night was semi-delirious. In the morning the pulse-beat was only 20 to 24 to the

[1] Gaz. Hebdom. de Méd. et de Chirurg., 1879, No. 38, p 599.

minute. What was particularly remarkable was a state of intermittent syncope which regularly followed the cardiac pulsations. Between two heart-beats the face grew pale, the eyes closed, and the lips blanched. A strong pulsation made the face and labial mucous membrane flush anew. This was so pronounced that without the slightest difficulty the pulse could be counted by observing the face alone. Upon auscultation there were heard the signs of an extensive dry pericarditis, a superficial double pericardial friction-sound. A systolic souffle, soft and prolonged, extended with equal intensity over the aortic and mitral areas. This condition lasted six days; during the first three days the pulse-rate remained unchanged, then it increased to 45 and the syncopal phenomena ceased. At the end of eight days the pulse had regained its normal rhythm and was 72. The pericarditis was favorably influenced by large and repeated blisters.

Blachez thought the bradycardia was intimately related with the inflammation of the serous membrane, probably to the more or less profound modification which the superficial muscular layers of the heart experienced from the pericarditis. The patient never had a complete attack of syncope, never an eclamptic seizure. Convalescence was slow.

Still another interesting case of rheumatic fever, with cardiac complications and bradycardia, has been recorded by Peacock.[1]

CASE IV.—A girl, aged twenty-four years; quite anæmic.

October 15. Rheumatic fever.

19*th*. Pulse 100. Skin hot and sweating. Pain and stiffness in back of neck, left shoulder and wrist and left ankle. Heart-sounds somewhat flat, without murmur; a sibilant rhonchus over all parts of chest.

22*d*. Better and freer from pain. Left ankle red, swollen, and tender. Pulse 60. Skin warm. Sweat copious, acid, and offensive. No heart murmur.

25*th*. Much better; still some pain in the right arm. Left hip, knee, and ankle painful. Pulse 42. The first sound of the heart somewhat prolonged. Severe pain in the cardiac region.

26*th*. Pulse 36. There was a somewhat harsh but low systolic murmur, most distinctly heard in the course of the pulmonary artery. Pains better.

November 2. Much improved and nearly free from pain. Tongue clear, somewhat dry. Pulse 36. Systolic murmur still audible to the left of the sternum at the third costal cartilage.

5*th*. Pulse 36, sharp; some pains over heart. Murmur more diffuse, but still intenser at the base and in the course of the pulmonary artery, not at the apex nor to the right of the sternum.

December 1. Patient well. Pulse 48, and steady. Murmur still audible at base.

28*th*. Pulse 60. Murmur entirely disappeared. Patient still chlorotic.

[1] Med. Times and Gaz., vol. i. p. 56, 1864.

Bouillaud[1] has also reported a similar but not so satisfactory case.

CASE V.—A young man, twenty-four years old. Fifth day of rheumatic fever. Decubitus dorsal. Severe pains in nearly all joints, especially in elbows and knees. Fever. Præcordial dulness five inches transversely, four inches vertically. Endo-pericarditis.

October 10. Pulse 92–96.

11*th*. Improvement. No pain in feet or knees. Shoulders more painful than elbows, but less so than yesterday. Skin bathed in sweat. No pain in præcordial region. Pulse 84.

15*th*. No improvement. Pulse 60.

16*th*. Pulse 56.

20*th*. Heart impulse felt over a considerable area. "A triple bruit," imitating the rhythm of "bruit de rappel." The first bruit constituted a murmur, the two others slight friction sounds.

22*d*. Cardiac dulness 4 inches 1 line transversely, 3 inches vertically. Pulse 44–48. The patient left the hospital perfectly well by the end of October.

A very interesting case of bradycardia in acute rheumatism with acute cardiac complications was observed by the late R. L. Macdonnell.[2]

CASE VI.—A merchant, aged forty-six years, with a history of previous rheumatism, was attacked with acute articular rheumatism on April 19, 1885. On the second day twenty grains of sodium salicylate were ordered to be given every fourth hour. This was continued until the tenth day (28th). The disease ran a typical course without discoverable cardiac symptoms until the sixteenth day, the pulse ranging from 100 down to 70–80. Upon this date the temperature was still slightly above normal. There was no albuminuria; no glycosuria. Toward evening he felt fatigued. At 7.30 o'clock there were ineffectual efforts to vomit, and the patient threw himself upon the bed, feeling faint. The breathing was steady at 20. The pulse beat strongly at 26, without irregularity or intermittence. He was weak and faint, but not unconscious. By 9 P.M. the pulse fell to 22.

May 5. (Seventeenth day.) 5.30 A.M. The pulse was 26. More comfortable and less weak. There was visible pulsation in the radial, ulnar and carotid arteries. Apex-beat in normal position. No thrill. No increase in the area of cardiac dulness. At the junction of the third costal cartilage with the sternum there was a soft, blowing systolic murmur which was not conducted over the normal aortic area, nor toward the apex, around the chest. The second sound was decidedly roughened. Later the pulse was 30.

6*th*. (Eighteenth day.) Condition improved. Pulse 58, steady and regular.

[1] Maladies du Cœur, vol. i. p. 509.

[2] Medical News, vol. xlviii., 1886, p. 432.

Murmur unchanged. Pain and swelling in right wrist. Nervous and hysterical. Slight nocturnal delirium. Evening temperature 102.4°.

7th. (Nineteenth day.) Pulse 70, intermittent, one beat in five. Condition of heart unchanged.

8th. (Twentieth day.) Pulse 90; temperature 101°; respiration 20. The murmur had disappeared.

Most writers upon diseases of the heart refer to the occasional slowing of heart-action in pericarditis, though, since the phenomenon is quite rare, specific examples of such occurrence are quite uncommon. Graves[1] had known the pulse to be less frequent than in health during the first stage of pericarditis. In his remarkable book, Ozanam[2] notes that a rare pulse at the beginning of an acute cardiac affection ordinarily indicates the invasion of pericarditis or of endocarditis. Here the phenomenon of slowness as contrasted with the ordinary pulse of inflammation is accounted for by an excitation of the vagus nerve. Similar observations have been made by a number of writers. Malherbe[3] saw three cases of acute pericarditis with rapid serous effusion, in which the respiratory movements were, speaking absolutely, more frequent than the beatings of the heart, there being 56 respirations per minute and 48 cardiac pulsations during the same interval in one case. In another case the beginning of the disorder was characterized for some days by malaise and dull pains in the præcordial region. Then, all of a sudden, violent pains developed in this region, with extreme anxiety and depression. The respirations were 64 to the minute, the pulse 52, feeble and depressed. The hand over the præcordial region felt no shock, but there was evident bulging and extended dulness. The heart-sounds were feeble and distant; they became a little stronger when the patient sat up, but the impulse was not more noticeable in the erect than the horizontal position. The resorption of the fluid was quite rapid and the pulse and respiration resumed their normal relation at the end of three days.

There are a number of recorded observations of bradycardia developing during the period of serous effusion into the pericardial sac. In his excellent paper, read before this Association in 1889 (and pub-

[1] Flint: Diseases of the Heart, 1859, p. 302.

[2] Le Circulation et le Pouls, Paris, 1886, p. 877.

[3] Journ. de la Sect. de Méd. de la Soc. Acad. du Départ. de la Loire Inf., vol. xxxi., 1855, p. 188.

lished in its *Transactions*), Dr. Prentiss presented abstracts of 91 cases of slow pulse which he had found recorded in medical literature. In two of these this condition was present. One was a case by Mayo,[1] a man, forty years old, with embarrassment of respiration supposed to be due to fluid in the pericardium, whose pulse-rate varied from 14 to 29. Recovery followed in two months. The other case was reported by Dr. James Russell,[2] whose patient also had embarrassed breathing attributed to pericardial effusion, and had a pulse-rate usually of 29, but upon some days as low as 14, and who recovered after three months.

It is evident that bradycardia occurring in acute rheumatism cannot, in all cases, be considered with the phenomena of convalescence from acute febrile disease, as Riegel, Bauer, and others are disposed to do; that it cannot be ascribed to an increased arterial tension occurring with the fall of temperature in connection with the general debility of convalescence, as Truffet would have it; or to heart exhaustion, as Traube has taught, whereby the resistance which the heart muscle opposes to its nervous motor apparatus in consequence of its exhaustion, is notably increased and the pulse frequency diminished, just as when the irritability of its inhibitory nervous system is increased. Where bradycardia develops during the active period of acute rheumatism it must be ascribed, doubtless, either to the specific influence of the disease acting through the blood directly upon the heart muscle itself, or upon its nerve elements, visceral or central, or to the stimulation of the cardiac nervous inhibitory apparatus, through inflammatory change in the heart muscle itself, directly or by extension, or in the endocardium, or pericardium, implicating the fibres of the vagus nerve. It is true, the usual effect of inflammation of any of these structures is increased frequency of heart action, yet it is widely admitted that inflammation of the pericardium at least may be the cause of unnatural slowness of this action. Slowing of the pulse is to be expected when the vagus nerve is directly involved in the inflammatory process, or is involved by pressure, or is irritated (Eichhorst[3]); and though myocarditis is also nearly always accompanied by quickened pulse, Bötticher found five cases of bradycardia in this condition.

[1] Lond. Med. Gazette, vol. xxii. N. S., p. 232.

[2] Med. Times and Gazette, 1877, ii. p. 60.

[3] Wiener med. Presse, 1881, xxii. p. 1381.

In view of the various factors that it is possible to imagine as provocative of bradycardia it would be unwise to deny the power of rheumatic principles circulating in the blood to slow the action of the heart, working upon the muscle itself or upon its nerves, as is assumed by Grob; and it would be equally unwise to assert that when bradycardia develops during acute rheumatism it may not depend upon rheumatic myocarditis, with or without endocardial or pericardial inflammation. At all events, in view of the clinical facts that have been adduced, it would seem not improbable that not only may the bradycardia that arises during the height of rheumatic fever, but, not unfrequently, that which occurs subsequent to the subsidence of this affection, be attributable to conditions in which the inhibitory nerve of the heart may be involved in irritation, and that, therefore, Traube's theory of "heart-tire" may not answer for all, even post-rheumatic bradycardia.

A possible source of fallacy in considering bradycardia is the influence of drugs. In many cases of rheumatism in which this symptom was noted, salicylic acid or salicylates had been given. When injected into the blood or given by the stomach in large quantities, salicylic acid may lower the pulse-rate (Brunton *et al.*). In the cases that have been observed, however, bradycardia developed in some where no salicylic preparation had been given, in some where the use of such agent had long been abandoned, and in some where the slow pulse was present before the first dose of salicylic preparation had been administered (Grob, Bötticher). Moreover, doses sufficiently large to slow the action of the heart are habitually larger than are demanded in the treatment of rheumatism. Both of my own cases, recorded here, had been taking digitalis before the appearance of bradycardia, the one for the arrest of epistaxis in combination with ergot and ipecac, the other for the correction of a very feeble, frequent, and intermittent heart-action. In the first case the dose was small, in the second it was moderate, and in both it was discontinued after a few doses. In the one bradycardia was present two weeks after digitalis had been discontinued, and in neither was there the slightest concomitant evidence of excessive action of the drug.

To sum up, the following conclusions are presented:

1. Bradycardia is observed rarely during the active stage of acute

inflammatory rheumatism. It occurs with greater frequency during convalescence from this disease.

2. When it occurs during convalescence, probably in most cases it is identical with bradycardia following acute febrile diseases of widely different nature, and directly the result of the febrile action itself upon the innervation or musculature of the heart.

3. When it occurs during the active stage of rheumatic fever it probably depends upon endocarditis or pericarditis or myocarditis (primary or secondary by extension), whereby the inhibitory nerves of the heart are implicated and consequently stimulated. Even where the physical signs of cardiac inflammation are absent, bradycardia occurring during the acute stage of rheumatism may be secondary to undetected myocarditis stimulating the vagus nerve.

4. It is possible, but exceedingly improbable, that this symptom may follow the action of the rheumatic *noxa* upon the cardiac muscle or nervous system directly.

DISCUSSION.

DR. PEPPER: If I remember rightly, when Dr. Prentiss presented his notable case of slow pulse, our attention was called to the rapidity of the respiration connected with the bradycardia. I do not know that Dr. Atkinson reports the rate of respiration in connection with the rate of pulse and with the temperature curve.

DR. ATKINSON: There was nothing notable in it. I had it recorded, but there was nothing remarkably disproportionate.

DR. PEPPER: I saw recently a very interesting case where, without any apparent cause, a middle aged man became the subject of "diaphragmatic palpitation"—I call it that for want of a better name—with bradycardia. He has attacks with respiration about 110, and pulse 50 or 60; he pants like a hunting dog after a chase, and keeps this up for hours, while able to go about and take food and sleep. During this time the pulse falls. I have some reason to think that there is a cervical pachymeningitis in the case.

Another case, which I mention to elicit discussion, and not as an important contribution, is that of a child with erysipelas of the face. There was a sudden recession of the erysipelas with development of all the symptoms of acute local peritonitis in the epigastric region and with bradycardia, in spite of rather high temperature. There was a gradual subsidence of the peri-

toneal symptoms and restoration of normal pulse, respiration, and temperature.

Such cases as Dr. Atkinson has quoted, of bradycardia with acute pericarditis, I am sure most of us are familiar with in our practices. I have seen a number of them. The whole subject, from its physiological standpoint of the way in which this is brought about, is an interesting and puzzling one.

DR. HENRY P. BOWDITCH, of Boston: The fact that the heart is connected to the central nervous system by two sets of nerve-fibres having antagonistic functions may make it difficult, in any given clinical case, to determine the mechanism of an alteration of rate of the heart-beat, for a stimulation of the accelerator fibres may have the same effect as a paralysis of the inhibitory fibres, and *vice versâ*, and in many cases it is impossible to decide whether we are dealing with a phenomenon of increased or diminished nerve-function.

DR. PEPPER: I should like to ask Dr. Ord as to his experience in London hospitals. I think that in our own hospitals we see much of this bradycardia succeeding acute illness in large, loose-fibred, muscular men. I do not know what the normal pulse-rate of stevedores and that class of men is, but I fancy it is rarely above 60 in health, and certainly the opportunity of finding a pulse of 52 or 54 is a common thing, as Dr. Atkinson has said.

DR. ORD, of London: Yes, one sees a great deal of slowing down of pulse after acute illness, particularly in people who are naturally robust. It has generally been put down to weakening of the whole system and weakening of the nervous system in particular. Dr. Atkinson's paper has for me an especial interest in that he draws attention to the occurrence of the slow pulse in acute rheumatism where the temperature is still raised. For many years it has been presented to me as not improbable, although I have no means of proving it as yet, that the pneumogastric nerve itself plays an important part in the phenomena of acute rheumatism. We see structures, the myocardium, the peri- and endocardium, with which it has important relations, taking on active inflammation quite out of all proportion, in many cases, to the intensity of the joint inflammation, but having, as Dr. Sibson showed, a very considerable relation with the temperature. It is a disease in which we observe a remarkable phenomenon in the skin—the skin acting profusely at the time when the fever is running high, and the perspiration not in any way relieving the severity, but rather adding to the aggravation of the symptoms. And we have the tendency, which we certainly see in London, to hyperpyrexia in this above all other diseases that one commonly meets with. All these have seemed to me to indicate that the system of the pneumogastric exercises at least an important part in the phenomena of acute rheumatism; whether through trophic nerve influence I cannot say.

For years, also, I have had the idea in my mind that acute rheumatism was to be regarded as the work of nerves excited in various ways—by strain, by reflex irritation; and I have thought that this would most probably ex-

plain the acute rheumatism which is apt to follow parturition, although I know that many people ably contend that this is rather a blood-poisoning than a result of reflex action. I should also include the acute rheumatism which occurs in lactation, or the acute rheumatism following an acute quinsy.

Recently, I have been making some observations which I should like to put before the world some day, and which I should hardly like to leave America without speaking of. During the last six or seven years, examining carefully a large number of cases of gastric ulcer in which anæmia was well marked, I have found physical signs which seemed to me to indicate the process of pericarditis with effusion; in many cases of endocarditis with distinctly an affection of the mitral valve, and sometimes of myocarditis. That is to say, I have had a series, mainly of young women between twenty and thirty years, very anæmic, and having the acute conditions of gastric ulcer (most frequently with marked hemorrhage), who all have increased upward cardiac dulness, particularly on the left side of the sternum, where it would reach the second costal cartilage, extending laterally to the left; extension of the impulse over the whole area, and, as I believe, friction-sounds associated. With these again, a frequent systolic murmur, extending to the axilla, and associated with accentuated second sound over the pulmonary valve. Of course, it may be that in these cases there is imperfect expansion of the lung, which allows the heart to come more fully in contact with the wall of the chest than it should. It may be objected to me that I have no post-mortems to record. Of course, that is my misfortune. If it be admitted that in these young women, without fever, without joint affection, there is a setting up of an endo- and probably a myocarditis in association with anæmia, how can we account for the inflammatory process coming about? I have for a long time thought that it came about through reflex irritation, conveyed up and down the fibres of the pneumogastric. Of course, it is possible that both the gastric ulcer and the cardiac mischief may be the result of the pneumogastric becoming irritated in an anæmic person. Or, lastly, they may all be lesions set going by anæmia. I have been inclined to think that anæmia itself is a condition which does predispose to affections of the myocardium; certainly, I have seen this occur more than once in pernicious anæmia.

Referring to Dr. Atkinson's cases, I should say the bradycardia here would fit in with the idea I have of the pneumogastric exercising some inciting function in acute rheumatism, and this is one more manifestation of the injury that it is working in the system at large.

DR. I. E. ATKINSON: I have to acknowledge with Dr. Bowditch, the extreme difficulty of reaching definite conclusions in regard to the way in which bradycardia is brought about. This is shown by the widely different conclusions reached by different persons. I have nothing to present in the way of a demonstration; still, it occurs to me, that during the active stage of rheumatism the changes that take place in the heart are due to a stimulating, and not to a paralyzing influence.

THE CLIMATE OF SOUTHERN CALIFORNIA FOR RESPIRATORY DISEASES.

A Preliminary Paper.

By NORMAN BRIDGE, A.M., M.D.,
PROFESSOR OF CLINICAL MEDICINE, ETC., IN RUSH MEDICAL COLLEGE, CHICAGO.

All climates with a maximum of sunshine and a dry atmosphere, if free from deleterious influences, have acquired a reputation for the cure of respiratory disorders, and this whether the climate is cold or warm. A great mass of favorable testimony has proven that there is substantial foundation for this reputation. But the good effect upon the sick of such climates cannot be wholly due to the elements named, nor to any purely climatic conditions; something must be credited to the fact of change—that patients are put under new conditions that are likely to act favorably upon them regardless of the special character of the climate. Pressure is brought to new physiological bearings able to sustain it, and relaxed from old ones, worn and fatigued; tissues and functions long forced to bear the brunt of the tension of life are relieved and allowed a long and needed rest and recuperation, while others are developed into new vigor by unwonted activity. The effects of these changes are similar in all climates not positively bad, and from any change patients may make from one place to another, and must not be lost sight of.

In estimating the effects of the beneficial elements peculiar to any climate of reputed value, one is confronted by the most pronounced bias for or against it, as well as the most absurd and incomprehensive inductions regarding its effect on the part of unprofessional persons who regard themselves as competent to speak, and sometimes on the part of professional men. Hence it is difficult to reach correct conclusions.

The climate of Southern California has had recorded in its favor

some remarkable cures of pulmonary disorders, hence the most fabulous curative properties are claimed for it for all such diseases. It is also condemned as a most undesirable climate. It is said to be a balmy, dry, health-giving clime; it is declared to be a cold, damp, and cold-inducing one.

It is always difficult to determine the effect of climate upon the sick, dissociated from all other influences; it is doubly so as to Southern California, that so many have sought for eternal sunshine and unvarying balminess, who have come with all sorts and degrees of respiratory diseases, some to recover, many to die.

Having made three visits to the region, the last extending through two-thirds of a year, and having endeavored to observe and fairly consider all attainable facts bearing on the fate there of cases of respiratory diseases, it seems to me that the following conclusions are justifiable:

A large number of cases of respiratory diseases migrating thither become greatly improved or substantially well. A part of these are chronic cases, some having existed for years; a part are acute cases that have existed too short a time to know what their fate might have been in the climates from which they came. But many cases fail of recovery or any marked improvement; many go rapidly or slowly forward to death as unfailingly as they could have done in the worst climate. The proportion between these two classes — those who recover and those who fail of improvement or die—it is manifestly impossible to know. But enough of the cases of undoubted grave pulmonary disease, like tuberculosis, recover or greatly improve to seem to establish some valuable influence which the patients experience in this region.

Cases of long standing are less likely to improve than those of recent origin, and if they do improve it is more slowly, requiring often a long residence to insure any approach to complete restoration. Among those that recover, although many are called cases of tuberculosis or consumption, a large majority are probably cases of non-tuberculous inflammation of the bronchial or peri-bronchial tissues, with or without throat complications. Such cases nearly always, sooner or later, improve or recover completely. But cases of true tuberculosis of the lungs do recover (and vastly more often than in our Eastern climates), and pass years without appreciable symptoms. The diag-

nosis of such cases is based in a few instances on a discovery of bacilli in the expectoration, unfortunately in more it must rely upon the occurrence of repeated hemorrhage and physical chest signs, taken in connection with a rational symptomatology.

The proportion of undoubted tuberculous cases recovering is small compared to the whole number seeking relief; possibly if more accurate diagnoses of all cases seeking relief were made, the proportion would be greater—possibly it would be even less than it now appears. Some of the cases of recovery are striking in the extreme.

As elsewhere, so here, pulmonary tuberculosis in children nearly always ends fatally. With adolescents and young adults the experience is not so bad, but it is unfavorable. The prospect of improvement is greatest for (1) those in mature years of life, with good heredity, good constitution and habits; for (2) those in whom the lesion is circumscribed in the lungs, and confined to them; better, if confined to one lung; and greatest of all for (3) such as fulfil the conditions named and seek the change in the incipiency of the disease.

It is a rule that has few exceptions, that tuberculous cases come here after they have lost in delay most of the hope of improvement from any climate or conditions. Most, but not all, of this misfortune is due to faulty diagnosis at the beginning. The vast majority of such cases of tuberculosis as come, leave their distant homes without an examination of the sputum for bacilli ever having been made; and, of course, those who come, or who are able to seek any climatic change, are a small proportion of the whole number of tuberculous patients. Of those cases in which tubercle bacilli are found by examinations made at home, and which afterward go to Southern California, this change is made too often after months of progress of the disease has left the patient with small hope of sustained improvement anywhere. The neglect on the part of practitioners to search early for bacilli is in part due to lack of facilities at hand or within reach for a proper examination; in part to neglect of the significance of the presence of bacilli; in part to a disbelief in their necessary connection with consumption. I cannot but regard the omission as more than deplorable—it is reprehensible in a high degree. It results in neglect or delay in the use of the best measures of relief, that costs many a poor fellow his life.

Tuberculosis may originate in Southern California, if the physio-

logical standard is lowered by heredity, disease, overwork, bad hygiene, depressing emotions, or any other debilitating influence. Quite a number of cases do originate, curiously as it may appear, from the cold of the winters. The winters are not cold; relatively they are warm, and in the sun, out of the wind, quite warm; but they are too cold to live indoors without artificial warmth unless one is both vigorous and in active exercise—conditions that are daily violated by large numbers of persons in their living and occupations.

While the climate has for invalids many advantages, it has some marked disadvantages. The most important one obtains with all dry climates—it is the great variation in temperature between day and night, sunshine and shadow. The dry atmosphere permits the passage of the sun's heat easily; in the sunshine it is always warm—out of the sun there is rapid radiation of heat and coolness by comparison. The difference between the reading of the thermometer in the shade and in the sun is much greater than in the moister climates of the East.[1] Patients and people, lulled by the idea of a mild climate, forget these facts, and often poorly clothe themselves and insufficiently heat their rooms, and so take cold, often to their permanent injury. The invalids rely too implicitly on the climate and often neglect all general hygiene, and good regimen even, and then wonder they are not well. The bad results of this neglect are more apparent in winter than in summer, but are apparent at all times. The temperature in winter, although not severe, and nearly always above the freezing-point, is yet cold enough for every person indoors, occupied or not, to have his room artificially heated, unless it receives a large volume of sunshine or unless he is freely exercising. Indoors in winter in Los Angeles it is no more true that artificial heat can safely be dispensed with, than it is in Chicago or New York—indeed it is quite as unsafe—for it is the ignoring of the degrees of cold slightly below safety, so characteristic of Southern California in winter, that leads to mischief; nobody ignores a zero temperature.

Strangers going to Southern California should, in the winter, wear

[1] Diathermancy of the air at Sierra Madre (sixteen miles north of Los Angeles). Average of repeated observations. Observations made early in the afternoon:

Elevation above sea-level 1250 feet. Difference between temperature in the shade and in the sun, standard thermometer, average 33° F. Difference as shown by black bulb thermometer incased in long test-tube, corked, average 74.5° F. Highest point registered by black bulb thermometer, average 162.5° F.

as thick underclothing as they do in the East, and in summer much thicker, and always, if possible, of wool; and they should wear woollen night-gowns. This course is most important for invalids, and cannot ever be neglected with safety. Living-rooms in winter should be kept as warm as is comfortable, and bedrooms should be slightly warmed, at least during the process of dressing and undressing.

There is a popular fear of night air in Southern California that leads many to occupy closed and unventilated rooms at night. The theory is erroneous and the habit most unfortunate; the night air is as good as the day air and considerably purer, only it is colder and demands the use of more clothing.[1]

Of the climatic influences that are beneficial, dryness of air is doubtless one—a fact that has been sufficiently enlarged upon. Another influence of this sort is the great amount of sunshine, the value of which is generally believed in, but just what the measure of its value is, dissociated from everything else, has hardly been made clear and would be difficult to demonstrate. There may be some unusual influence upon the system of the peculiar sunlight of this region and apart from the high diathermancy of the air, but it is unknown and must be a subject for further study and investigation. Much of the good influence often attributed to the sunshine is, in my view, to be credited to the out-door life which it enables patients to enjoy. The equability of the climate that enables patients to do this at all seasons is another force in the same direction and cannot be too much emphasized. Almost in the ratio of the time spent out-of-doors do patients receive benefit from this climate.

So remarkable appears to be the beneficial effect of the climate of Southern California upon certain cases of pulmonary tuberculosis that it seems probable there is some undetermined therapeutic element of air or light. The full effect of sunlight upon physiological processes is only partly explored, and the microörganisms of the air of the region in question have not heretofore received scientific attention. Studies are now under way in this last direction, but their results are, so far, not sufficient to justify their incorporation in this paper.

Different parts of Southern California differ in their value for pul-

[1] Of plates of agar jelly exposed by me to the air for five minutes at the close of the day and early in the morning (the close of the night), the former were found to develop nearly twice as many colonies of microörganisms as the latter.

monary diseases. The general opinion of the local profession seems to be borne out by experience that such cases do best some distance back from the seacoast, where the elevation is greater and the air dryer. Probably most points that fulfil these conditions are about equal in value. They differ, however, in their summer heat; at some of them this is at times extreme and depressing to the sick.

Many patients fail of the best results possible because, from theoretical considerations (and sorrowfully it must be said, sometimes on the advice of their doctors), they locate at points where the comforts of life and the proper regimen for the sick cannot be had, as well as where at times the heat is so great as to be decidedly depressing. The Colorado or Yuma desert is such a region, and some of the higher and more inaccessible points west of the mountains are nearly as bad. It is one of the first requisites for improvement for the average case that the patient be able to make himself thoroughly comfortable, be well fed with food that is proper for him, and that he be contented in his mind. In my short sojourn in the country I have seen quite a number of patients who have been practically killed by starvation, by discomfort from their environment, and by discontent —conditions that, in the main, were quite unnecessary.

REPORT OF TWO CASES OF EPILEPSY, WITH ALBUMINURIA, MISTAKEN FOR URÆMIC CONVULSIONS.

By JAMES TYSON, M.D.,
PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

It has happened to me within a comparatively short time to be consulted in two cases of albuminuria, associated with convulsions, which were supposed to be uræmic, but which proved to be true epileptic fits. The albuminuria in each case was responsible for the diagnosis made. In one of these cases two well-trained physicians were misled for a considerable time, and I held a like opinion with them until, in the course of a more prolonged study of the case, the truth dawned upon me. The second case was not so misleading from the outset, and with the light of my first was easily recognized.

Case I. was a married woman, aged fifty, who had had one child, a girl sixteen years old, at the time the case came under my notice. There was no sign of renal trouble during pregnancy, and no complication during or after labor. An aunt on the mother's side died of tubercular phthisis, and an aunt on the father's side of rapid consumption. The patient had one brother who was a confirmed epileptic. When seventeen years old, Mrs. H. had cough and hemorrhages, said to be from the lungs, for which she was treated with cod-liver oil. They ceased, and no other allied symptoms presented themselves. A few years before the illness about to be considered, she spat blood several times, but as she was approaching her climacteric her brother, who was a medical man, was not alarmed. In 1885 she had a spell of simple dysuria, the first in her life, which also passed off without any untoward effect apparent at the time.

On Saturday, December 11, 1886, she was attacked with severe headache, accompanied by great nausea. The headache was such as she had never before experienced. It continued for three days, but gradually abated, and by the 15th had nearly disappeared. At 8 o'clock on the evening of this day, however, she had a severe convulsion, during which she bit her tongue. She had a second at 12 o'clock, a third at 2 o'clock, and a fourth at 4 o'clock

in the morning. The convulsions were controlled by chloroform, used as seemed to be required.

The urine at this time was scanty, contained a small amount of albumin and some pus, but no tube-casts were found. The convulsions were regarded as uræmic, and she was placed upon a milk diet.

I was consulted concerning her on January 20th following (1887), when the urine was first sent to me for examination. It was a pale-yellow fluid, with a sp. gr. of 1015, feebly acid; contained a mere trace of albumin, and a small white sediment composed of pus and vaginal epithelium. No casts were found. I did not see her, however, until February 2, 1887, with Dr. William Savery and Dr. John W. Lodge. She was in bed for greater convenience of examination, but had been up, and indeed had not the aspect of a sick woman. Since her attack on December 15th she had been on a milk diet. The urine examined at this time (February 2d) was 1010, again contained a trace of albumin, and in the course of examining six slides I found two hyaline casts and one granular cast.

She continued to improve in general health without incident until a day or two previous to the 12th of March, when she had another attack of headache, less severe than the first, but accompanied by dizziness and noise in the ears. These symptoms gave rise to some apprehension, but were not followed by anything more serious. The urine was again examined; at this time it had a sp. gr. of 1015, contained a very decided sediment of pus, fully $\frac{1}{15}$ its bulk; again there was a very small quantity of albumin, but slightly more than at the previous examinations, $\frac{1}{50}$ then being noted. The increased albumin was reasonably explained by the increased amount of pus. In addition to the pus-cells, there were a few columnar cells, but no casts were found.

In the latter part of July, Mrs. H. had a rather severe attack of diarrhœa, in which I attended her, on account of the absence of her brother. It was ushered in by a sharp headache, and, as this had been the forerunner of her first attack of convulsions, some apprehension was again felt, and it was thought best not to check it too suddenly. No convulsion occurred, but after she had recovered, and was sitting up, her daughter described a sudden momentary unconsciousness, during which a fall was arrested by her opportune presence. This was on the 27th of August, 1887. An examination of the urine at this time discovered a sp. gr. of 1017, the same flocculent sediment composed of pus-cells and epithelium, a single undoubted hyaline cast, and the same small quantity of albumin.

On November 20th, she had a severe fit, on account of which I was called; but she had come out of it by the time I reached her, being, however, somewhat dazed. I saw her several times in the course of a couple of days, but there was no recurrence of the fit for nearly a year (September 20, 1888), although there was what was called "a threatening" a few days earlier. Other fits occurred December 22, 1888, April 8, 1889, and again December 6, 1889.

In the latter part of June, 1890, Mrs. H.'s attention was attracted by the

presence of blood in her urine, unattended at first by other symptoms. The hemorrhage continued until June 28th, when it had become quite copious. In my absence from the country, my friend, Dr. Horace Williams, was called. To the hæmaturia was now added severe pain over the region of the bladder and in the right flank. The urine, loaded with blood, became also very scanty, as small a twenty-four hours' quantity as twelve ounces being recorded.

Just when the bloody urine was assuming a brownish tint, the blood becoming replaced by pus, she had a slight chill, about 6.30 on the morning of the 2d of July, and at 5 o'clock the next morning a terrific chill, the temperature running up to 104.8°. By evening of the same day the temperature had fallen to 100.6°, and by the next morning was normal. All the symptoms then began to subside, and on the 9th of July she was sitting up. During the entire period of her serious illness there was no suggestion of a convulsion, while the ninety grains of potassium bromide which she had been taking daily for months had been discontinued, and at the end of ten days, when she was deemed thoroughly convalescent, she had a single epileptiform convulsion. About August 1st, she went to Wernersville, Pa., and while there, on August 18th, had a single typical convulsion, and two days later what the family called a "threatening," in which she lost consciousness for a few seconds only—analogous to other attacks referred to.

She, however, rapidly regained her health; and on examination of her urine by myself, September 23, 1890, it exhibited the same small sediment of pus and trace of albumin. Another examination in July revealed the same state of affairs. After the bromide was recommenced in the summer of 1890, she continued taking thirty grains three times a day.

On the 16th of June of this year I was sent for to see Mrs. H., because of a suspected attack of the usual kind, although she seemed not to have lost consciousness. There was no sign of anything wrong when I reached her. She is now apparently in good health, but has a shrinking, gentle manner which seems to me more or less characteristic of epileptics.

CASE II.—This patient, also a woman, Mrs. R., was forty-eight years old, and had four children. Her father died of apoplexy, and her mother of a tumor of the stomach. In childhood she had an attack of diphtheria, and was subject to sore-throat. Seventeen years ago, at the birth of her second child, there was albuminuria, but no other serious symptom, and the albumin soon disappeared from the urine. It, however, returned from time to time, but in the meantime a third child was born without albumin being discovered, and without other complication. No albuminuria was reported in her third pregnancy, nor in her fourth; but four months after the birth of her fourth and last child, and while in apparently perfect health, she had her first convulsion. This was eleven years ago. The fit was a very slight one, lasting but a few seconds; there was twitching and a smacking of lips, but she was scarcely unconscious. During the seven years that followed, she had about half a dozen more fits at odd intervals. In the four years subsequently she had none until January 1, 1890, when she had a very severe one, preceded

by what she calls dizziness, possibly an aura. From that date to September 12th, when I first saw her, she had no convulsion, nor has she had any to date.

At the suggestion of Dr. Brush she called upon me in September, 1890, and I elicited the above history. She described most of the attacks as being very short, and as consisting largely of what she described as a peculiar sensation lasting not more than a minute, during which she could hear her own voice making imperfect efforts at speech. The inability to speak properly continued several minutes after consciousness returned.

Her object in consulting me was to determine the nature of these attacks, the more especially as a distinguished member of this Association, whom she consulted in 1880, said she had Bright's disease, and would not live more than two years, probably only one. Ten years later she consulted Dr. Bartholow, of Philadelphia, who said that the attacks were epileptic. This view was held also by Dr. Brush, who sent her to me for an opinion.

In September, 1890, the evening and morning urine were examined on two separate occasions by myself, and each time a trace of albumin was found, but no sediment of any significance. The twenty-four hours' urine ranged from forty to fifty-four ounces.

Under the circumstances, I did not hesitate to declare the peculiar seizures to be epileptic, and that the albuminuria had nothing to do with them. With regard to the milder attacks, the question might indeed be raised as to whether they may not have been hysteroidal, and of the kind of which Dr. H. C. Wood says, in his book on *Nervous Diseases*, "They seem to be very close to epilepsy, and also to hysteria." Like these, their true character is to be determined by the history of the case and, in the present instance, the occurrence of more severe attacks of undoubted epileptic character. A recent letter from Mrs. R. informs me that she had none since the violent attack of January, 1890, although she had during the past winter the "dizzy turns" described.

In further illustration of the possibilities of the situation, my friend, Dr. J. Hendrie Lloyd, related to me lately his experience with a similar case. Toward bedtime one night he was sent for in great haste by the servants to see the head of a family with the ills of all the members of which he had supposed himself well acquainted. Responding promptly, he found the gentleman, who was past middle life, in terrific convulsions, which he at once concluded were uræmic. No others of the family except the servants were at home, and he could obtain no information. One attack succeeded another at close

intervals, during which the patient lay in a comatose or semi-comatose state. My friend was, however, able between two paroxysms to secure a specimen of urine. Hasty examination failed to discover albumin, but the constant association of contracted kidney with small and scarcely detectable albuminurias, only went to confirm his conclusion that he had to do with a case of uræmic convulsions. He remained throughout the night. The patient's wife was expected early in the morning, and he dreaded to meet her because of the sad prognosis he felt forced to make to her. He, however, gravely informed her of what had transpired, and she replied, with nonchalance, that he had been having similar attacks for twenty-five years!

Is there any way of avoiding similar errors? So far as any peculiarity of the convulsions themselves is concerned, I believe not. Uræmic convulsions differ in no way from epileptic convulsions. They are, in fact, typical epileptic convulsions, and exhibit the same varieties and degrees presented by such convulsions. In both the tongue is lacerated, both exhibit a degree of violence at once alarming and revolting. On the other hand, both may be so mild as to be barely noticeable, and both may be followed by periods of stupor of longer or shorter duration, or by a sudden return to the natural state. But true uræmic convulsions do not repeat themselves at intervals for months and even years at a time, and yet leave the patient apparently no worse for his or her experience. And if true epileptic convulsions happen to be accompanied by albuminuria, such albuminuria does not, as a rule, remain at a standstill or grow gradually less, but increases and is gradually associated with other phenomena of chronic Bright's disease, such as hypertrophy of the left ventricle, œdema, visual derangements, headache, high vascular tension, dyspeptic symptoms. When a history is obtainable of previous attack, it will generally be found that there has been a harmlessness of consequences following the pure epileptic convulsion which does not belong to the uræmic fit.

That such a complication of comparatively harmless epileptic seizures may be mistaken for the convulsions of Bright's disease, even where actual renal disease exists to some extent, must also be admitted. This is illustrated by Case I., where there is probably no inflammation of the pelvis of the kidney, extending thence into the interstitial tissue.

INDEX.

ANÆMIA, pathology of pernicious, 239
pernicious, of Texas cattle fever, changes in red blood-corpuscles in, 263
Atkinson, bradycardia in acute rheumatism, 292, 304.

BILLINGS, conditions and prospects of the Library of the Surgeon-General's Office, and of its Index Catalogue, 251
Blood-corpuscles, changes in red, in pernicious anæmia of Texas cattle fever, 263
Bowditch, bradycardia, 303
Bradycardia, case of, 258
in acute rheumatism, 292
Bridge, climate of Southern California for respiratory diseases, 305
Burr, pathology of pernicious anæmia, 239

CALIFORNIA, climate of Southern, for respiratory diseases, 305
Cattle fever, changes in red blood-corpuscles in pernicious anæmia of Texas, 263
Cholera, prevention of, in Glasgow, in 1866, 56
Convulsions, uræmic, and epilepsy, diagnosis of, 311
Councilman, arterial disease and tissue changes, 179, 199
diseases of the kidneys, 150

DA COSTA, intestinal perforation in typhoid fever, 214
Delafield on diseases of the kidney, 124

EDES, case of slow pulse, 258
Epilepsy and uræmic convulsions, diagnosis of, 311
Ernst, tuberculin and tuberculosis, 15

FITZ, intestinal perforation in typhoid fever, 200

GAIRDNER, arterial disease and visceral changes, 196
diseases of the kidney, 147
Library of the Surgeon-General's Office, 257
prevention of cholera in Glasgow, 56
results of removal of ovaries and tubes, 115

Glasgow, prevention of cholera in, 56
Graham, grave forms of purpura hæmorrhagica, 291
Griffith, pathology of pernicious anæmia, 289

HAIR, discoloration of, from use of pilocarpine and jaborandi, 262

INDEX Catalogue of the Library of the Surgeon-General's Office, 251
Intestinal perforation in typhoid fever, 200

JABORANDI, discoloration of hair from use of, 262
Jacobi, localization of phthisis in lungs, 54

KIDNEYS, on diseases of the, 124
Kinnicutt, treatment of tuberculosis by tuberculin, 1

LEE, results of removal of ovaries and tubes, 116
Library of the Surgeon-General's Office, 251
Lusk, remote results of removal of ovaries and tubes, 75, 118

MITCHELL, remote results of removal of ovaries and tubes, 113
Musser, grave forms of purpura hæmorrhagica, 279

NERVE-STRETCHING in trigeminal neuralgia, 119
Neuralgia, nerve-stretching in trigeminal, 119

ORD, arterial disease and tissue changes, 193, 195
    bradycardia, 303
    localization of phthisis in lungs, 52
Osler, Koch's treatment of tuberculosis, 35
Ovaries, remote results of removal of, 75, 86, 105

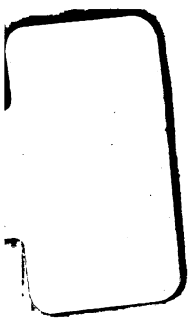
PEABODY, arterial disease and visceral changes, 154, 195
Pepper, bradycardia, 302, 303
    grave forms of purpura hæmorrhagica, 290, 291
    President's address, xv.
Phthisis, localization of, in upper lobes, 37
Pilocarpine, discoloration of hair from use of, 262
Prentiss, case of slow pulse, 258
    discoloration of hair from use of pilocarpine and jaborandi, 262
    grave forms of purpura hæmorrhagica, 291
Pulse, case of slow, 258
Purpura hæmorrhagica, grave forms of, 279
Putnam, remote results of removal of ovaries and tubes, 105

RHEUMATISM, bradycardia in acute, 292
Roosevelt, localization of phthisis in upper lobes, 37, 55

SINKLER, remote results of removal of ovaries and tubes, 86
Smith, A. H., diseases of the kidney, 145, 152
Theobald, changes in red blood corpuscles in pernicious anæmia of Texas cattle fever, 263
Stewart, nerve-stretching in inveterate trigeminal neuralgia, 119

TEXAS cattle fever, changes in red blood-corpuscles in pernicious anæmia of, 263
Tuberculin in treatment of tuberculosis, 1, 15, 35
Tuberculosis, treatment of, by tuberculin, 1, 15, 35
Typhoid fever, intestinal perforation in, 200
Tyson, diagnosis of epilepsy from uræmic convulsions, 311

URÆMIC convulsions and epilepsy, diagnosis of, 311

VAUGHAN, diseases of the kidney, 152
localization of phthisis in lungs, 53

WALCOTT, relations of drinking-water to disease, 216
Water, relations of drinking-, to disease, 216
Wathen, results of removal of ovaries and tubes, 117
Welch, changes in red blood-corpuscles in pernicious anæmia of Texas cattle fever, 263
grave forms of purpura hæmorrhagica, 290
localization of phthisis in lungs, 52